**Appendix B**

**Financial and Staffing Contributions of the Parties**

**For NIH**:

The NCI will conduct clinical and Non-Clinical Studies of Investigational Agent under its intramural and extramural research program and DCTD Clinical Support Assays as described in Appendix A. If Collaborator’s Investigational Agent is selected for the NCI-MATCH trial and Collaborator agrees to provide Investigational Agent, Collaborator will only be responsible for providing a sufficient supply of Investigational Agent for the cohort of patients to be treated with Collaborator’s Investigational Agent. No funding for regulatory support or correlative studies will be required from Collaborator. The NCI estimates that one to three person-years per year of effort will be dedicated to its participation in the Non-Clinical Studies, DCTD Clinical Support Assays, clinical studies, Steering Committee meetings, updates to its IND, compiling data, and drug management and monitoring in support of the clinical trials. PHS shall, in addition to its Principal Investigators provide sufficient staffing to execute and fulfill the obligations of the CRADA.

NCI will provide no funding to Collaborator for collaborative research and development pursuant to this CRADA, inasmuch as financial contributions by the U.S. government to non-Federal parties under a CRADA is prohibited under the Federal Technology Transfer Act of 1986 (15 U.S.C. 3710a(d)(1)).

**For Collaborator:**

*Personnel*:

Collaborator intends to commit one to three person-years per year of effort to permit the timely execution of the studies implemented under this CRADA. More specifically, this staffing shall include Collaborator full-time employees, consultants to the company, external contract agencies and contract research organizations. If Collaborator elects to perform any portion of the Research Plan through a contractor or consultant, Collaborator agrees to incorporate into such contract all provisions necessary to ensure that the work of such contractors or consultants is governed by the terms of the CRADA, including, but not limited to, the provision for the assignment of inventions of the contractor or consultant to Collaborator.

*Clinical Data Collection Support Funding Directly to Contractors:*

CTEP/DCTD utilizes the contract services of two companies for assistance in the monitoring of DCTD-sponsored clinical trials. Collaborator will be responsible for making arrangements directly with the appropriate DCTD contractors to receive reports from DCTD-sponsored trials. This will include quarterly reports, adverse event reports and summary reports. The contractor for the phase 2 and 3 studies will provide these reports electronically in a format compatible with Collaborator’s database. The NCI phase 1 contractor will also provide reports directly to Collaborator. Contact information for each of the DCTD contractors will be provided as needed. Any arrangement which involves the collection of more than the summarized data (Summary Data) provided annually to the DCTD will be at the expense of the Collaborator. Collaborator will make payment arrangements as necessary directly with such contractor(s).

Collaborator may make only reasonable requests for access to CRADA Data and Raw Data or any other information that is in the possession of NCI Extramural Investigators. The information will be provided according to a mutually agreed upon plan between the NCI, the Collaborator, and the NCI Extramural Investigator(s), and only in accordance with the guidelines and policies of the responsible Data Monitoring Committee. Collaborator will be responsible for the costs associated with any unusually burdensome requests, such as a request that the data be provided in a format which is different than that normally collected. Should Collaborator choose to review copies of patient case report forms, such a review will be at Collaborator’s expense and occur after notification and agreement of the NCI Extramural Investigators and only after all patient identifiers have been removed.

*Funding to NCI*:

1. CTEP/DCTD utilizes contract services for assistance in carrying out its responsibilities as a sponsor of clinical trials. Collaborator agrees to provide funding, as described in the table below, for each clinical trial submitted to a DCTD IND during the term of the CRADA to supplement the CTEP/DCTD support contract costs and other reasonable and necessary expenses incurred by NCI in carrying out its responsibilities under this CRADA as well as transportation and associated costs to support the participation of NCI staff at selected scientific or development meetings, where such participation will substantially foster development of Investigational Agent.

**NCI/DCTD/CTEP Cost Structure per Protocol/Year**

|  |  |  |
| --- | --- | --- |
|  | **Cost per Protocol per Year\*** | |
| **Phase** | **Cost** |  |
| **Pilot** | **$35,000** |  |
| **Phase 1** | **$35,000** |  |
| **Phase 1/2\*\*** | **$35,000** | **$50,000** |
| **Single arm phase 2 < 150 patients** | **$50,000** |  |
| **Randomized phase 2 or 3 up to 150 patients** | **$75,000** |  |
| **Randomized phase 2 or phase 3 150 to 300 patients** | **$100,000** |  |
| **Phase 3 300 to 600 patients** | **$150,000** |  |
| **Phase 3 > 600 patients** | **Negotiated** |  |
| **Organ Dysfunction** | **Negotiated** |  |
| **Registration trials/ Post marketing requirements/ SPA protocols** | **Negotiated** |  |
| \*Trial cost will be incurred for active studies- defined below. | | |
| \*\*Trial will initially be invoiced at lower phase initially, when trial moves to higher phase, the higher cost will be invoiced. | | |

The number of active clinical trials per year using Investigational Agent will not exceed XX and Collaborator’s funding to support the clinical trials will be up to a maximum of [$xxx,xxx] per year for the term of the CRADA. Funding for studies in excess of the XX clinical trials planned hereunder and that could be active at the same time will be by Amendment to the CRADA. Further, funding for large phase 3 clinical trials [with planned accrual over 600 patients], Organ Dysfunction trials, Registration Trials, Post Marketing Requirements and SPA Protocols will be negotiated by the Parties and added by Amendment to this CRADA.

For the purposes of this Agreement, active studies will be defined as those clinical trials conducted under this CRADA that are actively recruiting, treating, or have patients in follow-up per the Protocol. Completed studies will be defined as those clinical trials conducted under this CRADA where accrual has been completed and all patients have completed treatment and follow-up. However, in the event that a particular clinical trial is not enrolling on the predicted timeline, DCTD and Collaborator will discuss the appropriate steps prior to the due date of the applicable annual payment.

Collaborator and DCTD must mutually agree to the travel activities that are appropriate under this Agreement. Travel costs are limited by the Federal Travel Rules and Regulations for all government staff whether paid for by government funds or CRADA funds. Collaborator may provide direct support, under the 348 travel mechanism, for the travel and lodging costs for attendance of NCI staff at selected scientific or development meetings. Both Collaborator and NCI must agree that the activities would be appropriate under this Agreement and acceptance of Collaborator's support of NCI's participation in the activities will be contingent upon appropriate NCI approval. Travel costs for such travel are also limited by the Federal Travel Rules and Regulations for all government staff whether paid for by government funds or Collaborators.

1. Collaborator may provide up to [$100,000] per year during the term of the CRADA to support analytical assays, those focusing on identifying new assays for monitoring the biological activity of Investigational Agent and correlative studies associated with clinical Protocols which are approved by both Parties and made a part of the Research Plan. Such funds may be used for but are not limited to, costs of tissue biopsies, including sample acquisition, storage and shipping costs.
2. Collaborator also agrees to provide a one-time payment of [$20,000.00] for the initial IND filing during the term of the CRADA to support regulatory filings by CTEP and provide one-time payments of [$10,000.00] per investigational agent provided by Collaborator for additional IND filings to support any additional regulatory filings by CTEP.

Collaborator’s payment schedule will be as follows:

An initial payment of [$105,000] to be used to support the cost of the initial IND filing [$20,000], one phase 1 or phase 2 clinical trial [$35,000] and analytical/correlative studies [$50,000] will be due within 30 days of the execution of this CRADA.

At the end of each calendar year during the term of this CRADA, Collaborator will receive an invoice from NCI for funding to support activities (1) and (3) above. Collaborator will make a payment in January of the following year. The payment will be prorated for all studies activated or completed in the previous calendar year. The payment to support (3) above will be included in the invoice at the end of the year a DCTD IND is filed.

Collaborator will receive invoices during the term of the CRADA for funding needed to support the activities described in (2) above. Payment of these funds will be due within thirty days of receipt of the invoice in order to ensure continuation of the work.

Any additional funding will not be added to this CRADA without an appropriate written executed Amendment pursuant to Article 13.6.

No funds provided under this CRADA by Collaborator will be used by NCI to pay the salary of full-time tenured federal employees.

*Payment Information*:

Checks for monies payable directly to the NCI should be made payable to the National Cancer Institute and addressed to the individual identified under IC CRADA Notices on the Contacts Information Page.

All checks should be marked with a clear reference to the NCI CRADA Number and Title: CRADA # “xxxx”. Should NCI require electronic deposit of any monies payable under this CRADA NCI agrees to provide Collaborator with the appropriate account information.

*Materials/Equipment Contributions:*

NCI will not provide to Collaborator IC Materials to Collaborator for use under this CRADA and Collaborator will not provide to IC Collaborator Materials for use under this CRADA. If NCI decides to provide to Collaborator IC Materials for use under this CRADA, or if Collaborator decides to provide to IC Collaborator Materials for use under this CRADA, those materials will be transferred under a cover letter that identifies them and states that they are being provided under the terms of the CRADA. Collaborator will not provide capital equipment for use under this CRADA.