**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 as described in Appendix A. The NCI estimates that one to three person-years per year of effort will be dedicated to its participation in the Non-Clinical Studies, 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 NIH CRADA Extramural Investigator/Officer(s) 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 Safety Monitoring Board. 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. **Clinical Trials Support.** 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** | **$150,000 + Negotiated** |  |
| **Organ Dysfunction** | **Negotiated** |  |
| **Registration trials/ Post marketing requirements/ SPA protocols** | **$150,000 + Negotiated** |  |
| \*Trial cost will be incurred for active studies- defined below. | | |
| \*\*Trial will be invoiced at lower phase initially, when trial moves to higher phase, the higher cost will be invoiced. | | |

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 upon both Parties’ agreement, will be invoiced by NCI as described below.

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. Reduced fees will also be negotiated for any trial that has a few remaining patients receiving treatment on a trial.

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 Collaborator funds.

1. **Regulatory Support.** Collaborator 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.
2. **Correlative Studies Support.** Collaborator agrees to provide funding to support non-clinical studies such as Biomarker studies, analytical assays, studies focusing on identifying new assays for monitoring the safety and biological activity of Investigational Agent, pharmacokinetics (PK) studies and correlative studies (collectively “Correlative Studies”) associated with clinical Protocols which are approved by both Parties and made a part of the Research Plan. For purpose of this paragraph, Collaborator agrees that the Correlative Studies Support may also be used for but is not limited to, costs of tissue biopsies, including sample acquisition, storage and shipping costs, as well as additional medical examinations such as ophthalmic exams, echocardiograms and blood tests associated with the administration and monitoring of the Investigational Agent used in a Protocol. The Parties acknowledge that accurate cost estimates for these studies may not be available at the time of the CRADA execution because Protocols may not be finalized. NCI suggests that Collaborator budget $100,000.00 to $150,000.00 per clinical Protocol in its CRADA budget plan in order to be ready to provide the Correlative Studies Support for mutually agreed upon Correlative Studies when requested by NCI to avoid delay in conducting the Protocol. More detailed estimates of the Correlative Studies Support will be available when a specific clinical Protocol is approved by both Parties. Collaborator funding will be adjusted accordingly if the NCI Investigators are able to secure additional funding from other sources. In addition, NCI will review the Collaborator Correlative Studies Support from time to time so that the invoices Collaborators receives reflect the funds needed to support the Correlative Studies.

(4) If Collaborator’s Investigational Agent is selected for the NCI-MATCH trial and/or NCI pediatric MATCH trial, and Collaborator agrees to provide Investigational Agent, Collaborator will be responsible for providing a sufficient supply of Investigational Agent for the cohort(s) of patients to be treated with Collaborator’s Investigational Agent. No funding will be required from Collaborator to support funding items (1) Clinical Trials Support and (2) Regulatory Support above for the NCI MATCH and NCI pediatric MATCH subprotocols. However, Collaborator may be required to provide for item (3) Correlative Studies Support as described above, for patients enrolled in the mutually approved subprotocols until the completion of these protocols.

(5) If Collaborator’s Investigational Agent is approved for use for a non-CTEP IND trial, Collaborator will only be required to provide the Investigational Agent for the trial. No support funding will be collected by NCI for such studies.

Collaborator’s payment schedule will be as follows:

An initial payment of [$120,000] will be due within 30 days of the execution of this CRADA. The Payment will be used to support funding item (1) Clinical Trials Support, $50,000.00; funding item (2) Regulatory Support, $20,000.00; and funding item (3) Correlative Studies Support, $50,000.00.

At the end of each calendar year during the term of this CRADA, if the initial funds above have been depleted or are projected by CTEP to be insufficient to continue the CRADA Research Plan, Collaborator will receive an invoice from NCI for funding to support funding items (1) Clinical Trials Support and (3) Correlative Studies Support above. Collaborator payments will be due 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 (2) above will be included in the invoice at the end of the year a DCTD IND is filed.

Payment of these funds will be due within thirty days of receipt of the invoice in order to ensure continuation of the work.

The funds provided by Collaborator will be deposited by NCI into separated accounts to support the intended activities. However, Collaborator agrees that funds for (1) Clinical Trials Support, (2) Regulatory Support and (3) Correlative Studies Support may be transferred by NCI between the accounts if necessary to ensure that clinical trials are not delayed. 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, “xxxxxx”. 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 NCI Materials to Collaborator for use under this CRADA and Collaborator will not provide to NCI 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 NCI 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.