|  |  |  |
| --- | --- | --- |
|  | **NCI Formulary**  **LETTER OF INTENT**  **Submission Form v1.0** |  |
| **National Cancer Institute**  **Division of Cancer Treatment and Diagnosis**  **Cancer Therapy Evaluation Program** | |

*To complete the form electronically, use the mouse pointer or the Tab key to navigate. Select and enter text for each text field.*

|  |  |
| --- | --- |
| Institution: | [Click and enter Institution] |
| Institution Code1: | [Institution Code] |
| Other Trial Team Sites1: | [Click and enter Other Clinical Sites/Institution Codes]  [Click and enter Translational Sites] |
| Title of LOI : | [Click here to enter Title] |
| LOI Version Submission Date: | [Click here to enter Date of submission to PIO] |
| Agent(s)supplied by the NCI Formulary1: | [Click and enter NCI Formulary Agent] |
| Commercial Agent(s)/Source: | [Click here to enter Commercial Agents] [Click and enter Source] |
| Tumor Type:  *(Click within the [[ ]] and type ‘x’ to indicate the tumor type)* | [[ ]] Solid Tumor  [[ ]] Hematologic Malignancy (NOS)  [[ ]] Disease-Specific |
| Disease-Specific1:  *(Specify the Name and Code of the Study Disease)* | 1. [Click and enter Disease Name] [Click and enter Disease Code]  2. [Click and enter Disease Name] [Click and enter Disease Code]  3. [Click and enter Disease Name] [Click and enter Disease Code] |
| Phase of Study: | [Click and enter Study Phase] |
| Estimated Monthly Accrual:  *(****Note****: Projected accrual rates should be realistic. Actual accrual will be monitored and measured against this accrual estimate, and failure to meet accrual goals may result in study closure. )* | [Click and enter Accrual] |
| Proposed Sample Size: | Minimum: [Click and enter Size] Maximum: [Click and enter Size] |
| Earliest date the study can begin: | [Click and enter Date] |
| Projected Accrual Dates: | *Document in Appendix A.* |
| If yes, provide the Award Number: | [Click and enter Award Number] |

|  |  |
| --- | --- |
| What is the source of funding for the trial? Will funding be requested from the company supplying the Formulary agent? If so, how much and for what purpose? | [Click and enter source of funding] |
| Will an investigational laboratory assay be used as an integral biomarker in the trial?2 | [Click and enter Y or N] |
| If yes, indicate all integral investigational laboratory assay(s) and the purpose(s) for each one: e.g., eligibility criterion, assignment to treatment, stratification variable, risk classifier or score, other (describe in detail).2  (If the investigational assay(s) is used for medical decision-making [or treatment-directing], then this LOI and supporting documentation may be forwarded to the Office of In Vitro Diagnostics and Radiological Health (OIR)/FDA for review. If the assay(s) has/have already been presented to OIR/FDA, then please denote.) | [Click and enter name of each integral biomarker and describe purpose and other details in Correlates table below] |
| If the proposed trial includes correlative studies, indicate whether there is currently funding for them. | [Click and enter Y or N] |
| If yes, provide funding source for each correlative study. If funding is available for some, but not all, correlatives, please indicate. | [List correlatives and provide funding source (e.g., grant number if applicable) for each] |
| If no, will funding for correlative studies be sought? | [Click and enter Y or N] |

|  |  |  |  |
| --- | --- | --- | --- |
|  | | | |
| Principal Investigator (PI) Name: | [Click and type Your Full Name to certify the submission] | Date: | [Click and enter Date] |
| PI Street Address: | [Click and enter Room/Suite/Dept.] | | |
| [Click and enter Street Address] | | |
| [Click and enter City, State, Postal Code] | | |
| PI Phone: | [Click and enter Phone No.] | | |
| PI Fax: | [Click and enter Fax No.] | | |
| PI E-mail: | [Click and enter E-mail Address] | | |
| The Principal Investigator agrees to accept Confidential Information, such as the Investigator Brochure and any other shared information, and employ all reasonable efforts to maintain the Confidential Information secret and confidential, such efforts to be no less than the degree of care employed by the Principal Investigator/Institution (the receiving Party) to preserve and safeguard its own confidential information. The Confidential Information of the NCI and Pharmaceutical Collaborator (the disclosing Parties) shall not be disclosed, revealed, or given to anyone by the receiving Party except individuals working on behalf of the receiving Party who are under an obligation of confidentiality to the receiving Party and who have a need to review the Confidential Information in connection with the receiving Party's evaluation. Such individuals shall be advised by the receiving Party of the confidential nature of the Confidential Information and that the Confidential Information shall be treated accordingly. By submission of this NCI Formulary LOI Form, the Principal Investigator agrees to this statement. | | | |
| Authorized Institutional Official Name: | [Click and type Your Full Name to certify the submission] | Date: | [Click and enter Date] |
| Institutional Official Address: | [Click and enter Room/Suite/Dept.] | | |
| [Click and enter Street Address] | | |
| [Click and enter City, State, Postal Code] | | |
| Institutional Official Phone: | [Click and enter Phone No.] | | |
| Institutional Official Fax: | [Click and enter Fax No.] | | |
| Institutional Official E-mail: | [Click and enter E-mail Address] | | |
| Please submit NCI Formulary LOIs to the Protocol Information Office (PIO) via e-mail at:  [**pio@ctep.nci.nih.gov**](mailto:pio@ctep.nci.nih.gov)**, Attention: Formulary LOI**  **Notes**: Questions? Please e-mail the NCI Formulary LOI Coordinator at [pio@ctep.nci.nih.gov](mailto:PIO@CTEP.NCI.NIH.GOV). | | | |

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

(Principal Investigator Signature) Date

|  |
| --- |
| **Rationale and Background:** *(This section should provide the study rationale and supporting preclinical and/or clinical data and address the following: what is the unmet need, why the patient population was chosen, why the drug or drug combination was chosen and any potential safety concerns with the drugs or drug combination, and how the study results might impact future trials/practice. The background information should be limited to what is relevant to the proposed study and should be presented succinctly but with sufficient detail to enable evaluation by the reviewers. Avoid indiscriminate cutting-and-pasting from investigator brochures, trial solicitations, or other CTEP communications.)*  [Click and enter Background] |
| **Hypotheses:** *(Succinctly state the hypothesis for each primary and secondary objective.)*  [Click and enter Rationale/Hypotheses] |
| **Objectives:** *(List primary and secondary objectives. Ensure that the study design allows for these objectives to be met and that the statistical plan provides an adequate plan to analyze or describe the data for each objective.)*  [Click and enter Objectives] |
| **Abbreviated Eligibility Criteria:** *(Provide key inclusion criteria. These should include patient age, performance status, whether abnormal organ function is permitted [if Yes, list only abnormal organ function parameters], permissible and required prior therapy, tumor type, and integral markers, if applicable.)*  [Click and enter Eligibility Criteria] |
| **Study Design:** *(Succinctly describe the general study design. If applicable, describe randomization and/or stratification. A schema or flow diagram may be used, if appropriate. If the trial involves biomarker studies, the Biomarkers Table below* ***must*** *be filled out according to the instructions. Appendices detailing the biomarker assays may be required as well. Please read the instructions carefully.)*  [Click and enter Study Design] |
| **Treatment Plan:** *(State the dose, method of administration, and schedule of each drug, and, if phase 1, provide the dose escalation scheme, and definitions of DLTs. State the duration of treatment, the duration of the study, and the duration of follow-up.)*  [Click and enter Plan] |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Correlates:** *For* ***all*** *correlates, whether integral, integrated, or exploratory, and whether or not CTEP support will be requested, provide text in an appendix describing them and complete the* ***Biomarkers Table*** *below. Refer to footnote, page 2, for definitions of integral and integrated biomarker tests. All other biomarker tests are considered exploratory. In the table, provide the name of the lead PI for each correlate and his/her site. In the column labeled “M/O”, indicate with “M” or “O” if specimen collection or imaging test is either* ***M****andatory or* ***O****ptional. If the assay result will be reported to the patient or the patient’s physician at any time, on or off study, the assay must be performed at a CLIA-approved laboratory. For all correlates, provide a* ***letter of commitment*** *from the collaborating laboratory.*  *An integral biomarker is one that is inherent to the design of the trial and must be measured in real-time for the trial to proceed. An integral assay that will be used to determine eligibility or treatment may need to be performed under an Investigational Device Exemption (IDE) from the FDA.*  *Integrated biomarkers are defined as tests that are designed to test a hypothesis, not to generate hypotheses. The integrated biomarker assay already should have been tested in human subjects and demonstrated reproducible analytic qualities.*  ***(Note: For LOI review, each biomarker assay intended for inclusion in the study must be entered into the table below, and all fields must be completed)***  **Biomarkers Table\***   | **Biomarker Namea**  **AND Lead PI and Site** | **Assay**  **(CLIA: Y/N)** | **Use (Integral, Integrated, or Exploratory)AND Purpose b** | **Tissue/Body Fluid Tested**  **and Timing of Assay** | **M/O** | **Funding Source(s) c** | | --- | --- | --- | --- | --- | --- | | [Click and enter Biomarker(s)]  [Click and enter Lead PI/Site] | [Click and enter Assay]  CLIA: | [Click and enter Use]  [Click and enter Purpose] | [Click and enter Tissue/Fluid]  [Click and enter Timing] |  | [Click and enter Funding Source] | | [Click and enter Biomarker(s)]  [Click and enter Lead PI/Site] | [Click and enter Assay]  CLIA: | [Click and enter Use]  [Click and enter Purpose] | [Click and enter Tissue/Fluid]  [Click and enter Timing] |  | [Click and enter Funding Source] | | [Click and enter Biomarker(s)]  [Click and enter Lead PI/Site] | [Click and enter Assay]  CLIA: | [Click and enter Use]  [Click and enter Purpose] | [Click and enter Tissue/Fluid]  [Click and enter Timing] |  | [Click and enter Funding Source] | | [Click and enter Biomarker(s)]  [Click and enter Lead PI/Site] | [Click and enter Assay]  CLIA: | [Click and enter Use]  [Click and enter Purpose] | [Click and enter Tissue/Fluid]  [Click and enter Timing] |  | [Click and enter Funding Source] |   *\* Insert additional rows as needed.*  *a Multiple biomarkers may be listed in the same row if they are performed using the same assay in the same laboratory by the same investigator. This field may also specify a panel (e.g., BROCA); individual markers in the panel may be listed in Appendix B.*  *b Briefly specify the role of the biomarker in the study (e.g., eligibility criterion, assignment to treatment, stratification factor, response assessment, prospective research, hypothesis generation, etc.). If a hypothesis will be tested, please succinctly state it (e.g., “to identify biomarkers of response”).*  *c Indicate all funding sources.* |
| **Imaging Correlates Table\***   | **Correlative Objective**  **(Name of Correlate & Lead PI and Site)** | **Imaging Technique** | **Organ(s) Scanned and Timing of Scans** | **M/O** | | --- | --- | --- | --- | |  |  |  |  | |  |  |  |  | |  |  |  |  |   *\* Insert additional rows as needed* |
| **Endpoints/Statistical Considerations:** *(State explicitly the null and alternative hypothesis(es) for the primary objective(s). Also state the sample size and associated type I and type II errors. Provide an analysis plan for both primary and secondary objectives, including correlatives. Include information about which statistical tests will be applied. State the projected accrual rate and ensure that the accrual goals are realistic and achievable with current resources.)*  [Click and enter Endpoints] |
| **References:** *(Provide references for cited data and key background/concepts. Verify all references.)*  [Click and enter References] |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Projected Accrual:**  *Projected accrual rates should be realistic. Actual accrual will be monitored and measured against this accrual estimate and failure to meet accrual goals may result in study closure.*  ***Note: Failure to provide sufficient information for NCI reviewers to evaluate the ability to attain projected accrual may delay approval of the LOI.***  **Overall Study Projected Accrual Table**   | **Total Projected Accrual** | [Click and enter Number] | | --- | --- | | **Projected Start Date** | [Enter Month] / [Enter Year] | | **Projected End Date** | [Enter Month] / [Enter Year] | |

**Appendix A – Projected Accrual & Competing Trials**

**Appendix B – Correlative and Biomarker Assay Description(s)**

*Details of biomarker assays may be provided here.*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **FORMULARY CRADA: Cost Estimate Worksheet** | | | | | | |
|  |  |  |  |  | **PERIOD OF PERFORMANCE** | |
| Title | |  | Date |  | **FROM** | **THROUGH** |
|  |  |  |  |  | date of award | "x" months after date of award |
| **DIRECT LABOR** | |  |  |  |  |  |
| LABOR CATEGORY | HOURLY RATE | # OF HRS. | TOTAL SALARY | FRINGE % | FRINGE AMOUNT | TOTAL DIRECT LABOR |
|  |  |  | $0.00 |  | $0.00 | $0.00 |
|  |  |  | $0.00 |  | $0.00 | $0.00 |
|  |  |  | $0.00 |  | $0.00 | $0.00 |
|  |  |  | $0.00 |  | $0.00 | $0.00 |
|  |  |  | $0.00 |  | $0.00 | $0.00 |
|  |  |  |  |  | **SUBTOTAL DIRECT LABOR** | $0.00 |
| **OTHER DIRECT COSTS:** | | |  |  |  |  |
| **CONSULTANT/SUBCONTRACT COSTS** | | | | | |  |
| *(List names and services to be provided - attach agreement and pricing)* | | | | |  |  |
|  |  |  |  |  |  |  |
| **EQUIPMENT** |  |  |  |  |  |  |
| *(Provide description and price for each item)* | |  |  |  |  |  |
|  |  |  |  |  |  |  |
| **SUPPLIES** |  |  |  |  |  |  |
| *(Provide itemized list with prices)* | |  |  |  |  |  |
|  |  |  |  |  |  |  |
| **PATIENT CARE COSTS** |  |  | Estimated cost |  |  |  |
|  | | | | |  |  |
|  |  |  |  |  |  |  |
| **OTHER DIRECT COSTS** |  |  |  |  |  |  |
| *(Provide itemized list with prices)* | |  |  |  |  |  |
|  |  |  |  |  | **SUBTOTAL OTHER DIRECT COSTS** | $ |
| **TOTAL DIRECT COSTS** | | | | | | $ |
| *(Subtotal Direct Labor + Other Direct Costs)* | | | | | |  |
| **INDIRECT COSTS OR OVERHEAD ( )%** | | | | | |  |
| *(May only be applied to non-patient care related costs)* | | | | | |  |
| **TOTAL COSTS** | | | | | | $ |
| *(Total Direct costs + Indirect Costs)* | | | | | |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |