**Non-Confidential – Combinations Alliance Expression of Interest Form Guidance Notes**

These are guidance notes for investigators before completing your Expression of Interest (EOI) form to provide the relevant details summarising your EOI.

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| **Criteria for Inclusion** |
| Background | Strong scientific and clinical rationale |
|  | Relevant preclinical data and/or proposals for associated preclinical work to support the combination |
|  | Lack of overlapping toxicity  |
|  | Minimal or no existing trial data and no ongoing/competing trials |
|  | Not on company sponsored development path or other investigator led trials |
| Development Strategy | Patient population is accessible |
|  | Sponsorship and operational management confirmed *(preferred)* |
|  | CTU capacity  |
|  | Developability of proposal is considered |
|  | Capability to open study within 12 months of CRC |
| CSG Support | CSG/sub-group support prior to workshop *(preferred)* |
| ECMC Support | ECMC lead supports the proposal |
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| **Combinations Alliance Requirements** |
| Phase Ib/IIa | Primary endpoint: Safety, tolerability, PK of combo |
|  | Secondary endpoint: Non-statistically powered efficacy (preferably biomarkers) |
| Dose escalation  | 2-4 cohorts |
|  | 3-6 pts/cohort |
| Dose expansion  | Dose expansion numbers should be justified according to indication to further characterise the safety and/or preliminary efficacy of the combination |
| Combination  | Essential, e.g., radiotherapy, SoC, novel:novel |
| Sites  | ECMC (from or affiliation with an ECMC) collaboration 2-4 sites |
| Funding Committee | CRUK’s Clinical Research Committee (CRC) |
| Sponsorship | Academic sponsorship capability and engagement by the Chief Investigator(s) with the Sponsor and key collaborators at concept development and throughout |

**Note on Delivery:**

The success of these Alliances is dependent on the timely EOI development and clinical trial delivery. We highly recommend that the intended Sponsor, Research & Development (R&D) and Clinical Trial Unit (CTU) that would support the proposed trial is involved as early as possible to achieve the following delivery timelines.

Expected delivery: CRC approval - Trial submissions: 8 months

Trial approvals- 1st centre open: 4 months

First centre open - first patient randomisation: 4 weeks

**Note on Confidentiality:**

Only non-confidential information should be included in the EOI proposal. If confidential data exists that would strengthen the rationale or other aspects of the proposal, the author can/should emphasise that a statement is supported by confidential information the author is able to share, but only under a Confidential Disclosure Agreement (CDA). If the company finds the non-confidential EOI proposal sufficiently intriguing, execution of a CDA so that information can be considered will be discussed.

**Note on the use of model based approaches**:

The JSC will assess on a trial by trial basis whether it is appropriate to consider a model based approach within the trial design. If advice is not available locally we recommend that you contact the MRC Hubs for Trial Methodology Research, who offer a Methodology Advisory Service for Trials (MAST). For more information on how to contact MAST, visit: <http://methodologyhubs.mrc.ac.uk/advice/methodology-advice/>