Applicants seeking funding for **hit to lead and lead optimisation to candidate selection** should complete this supplement in addition to the Case for Support form and upload to Je-S under document type Supporting Data (for further information, please refer to the DPFS Guidance for Applicants).

The layout of the form is intended to allow clear presentation of the current status of the project and development plan if funded. The information provided in both this supplement and Case for Support will be used by Panel Members when assessing the proposals. There is no requirement to duplicate or reiterate large elements of information between the forms; where responses to questions are duplicative, please include a cross-reference.

### Confidentiality

Information provided in the form will be treated in the strictest confidence and will not be made public or published. All Panel Members and External Peer Reviewers who review the proposal will have signed confidentiality agreements.

### Project Information

As per the information given in your Case for Support form and Je-S submission:

|  |  |
| --- | --- |
| **Principal Investigator** |  |
| **Institution** |  |
| **Project Title** |  |

### Target Product Profile (TPP) / Key Target Compound Parameters of the proposed Investigational New Drug (IND)

Max 20 words per answer (if known / best guess at this stage). Please note that this information will be assessed in conjunction with the information provided in the Case for Support; the responses here should focus on the hoped-for properties of the proposed IND.

|  |  |
| --- | --- |
| Target name |  |
| Mechanism of Action  *e.g. agonist, antagonist* |  |
| Route of Administration  *e.g. oral, IV, topical etc* |  |
| Duration of Treatment  *e.g. acute, chronic* |  |
| Dosage Regimen  *e.g. 2x daily* |  |

### Structures and Data

Please provide structures for the most promising chemical series being actively developed. Failure to include chemical structures may negatively impact the ability of the Panel to assess the suitability / strengths of your proposed chemistry plan. In subsequent sections, please summarise the available data in the same columnto allow the answers to be read as a table. Data are requested for any available assays for the lead molecule shown and the range seen within the chemical series, including (but not limited to): biological assays, physicochemical properties, liabilities and development risks for up to two chemotypes / chemical series.

|  |  |  |
| --- | --- | --- |
|  | **Chemotype / Series 1** | **Chemotype / Series 2** |
| **Lead Structures** | *Draw chemical structure of lead* | *Draw chemical structure of lead* |
| **Physicochemical Properties** | | |
| *e.g. Molecular weight* |  |  |
| *e.g. clogP* |  |  |
| *e.g. PSA* |  |  |
| *e.g. Solubility* |  |  |
| *e.g. Stability (solution & solid)* |  |  |
| *e.g. Heavy Atom Count (HAC)* |  |  |
| *e.g. Number of Hydrogen Bond Donors and Acceptors (HBD/A)* |  |  |
| ***In vitro* Biological Activity** | | |
| *e.g. Primary assay #1* |  |  |
| *e.g. Primary assay #2* |  |  |
| *e.g. Secondary assay #1* |  |  |
| *e.g. Selectivity assay #1* |  |  |
| ***In vitro* DMPK Assays** | | |
| *e.g. Permeability (if applicable)* |  |  |
| *e.g. Microsomal clearance* |  |  |
| *e.g. CYP450 inhibition* |  |  |
| *e.g. Plasma protein binding* |  |  |
| ***In vivo* DMPK Assays** | | |
| *e.g. Plasma clearance [& Species]* |  |  |
| *e.g. Fpo (%) [& Species] (if applicable)* |  |  |
| *e.g. Route of clearance* |  |  |
| **Toxicology / Safety Assays** | | |
| *e.g. Genotoxicity* |  |  |
| *e.g. hERG binding* |  |  |
| *e.g. Receptor/channel panel screening* |  |  |
| *e.g. cytotoxicity studies* |  |  |
| ***In vivo* Data (if available)** | | |
| *e.g. Tolerability studies* |  |  |
| *e.g. Biomarker assay and dose to produce biomarker modulation* |  |  |
| e.g. *Dose to produce efficacy* |  |  |

**Project Tractability**

Summarise the main structure activity / property relationships for each chemical series (max 300 words).

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Highlight the key challenges to optimisation of the series towards the TPP and outline how these will be addressed (max 300 words).

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Describe the biological assays and models to be used in the project including their duration and throughput where relevant (max 300 words).

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Explain how risks associated with the translation between *in vitro* assays, *in vivo* models, and activity in humans will be minimised (max 300 words).

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