

NOTE: This PDF is for reference only and is not submittable. To submit a Concept Stage proposal, please visit <https://vitalhubhealth.com/smart-antiviral-prize/> and click “Apply Now.”

Concept Paper - Required Sections

The SMART Antiviral Prize focuses on the discovery and early development of orally bioavailable small-molecule antiviral therapeutics that support scalable and rapid outbreak response efforts. For the purposes of this solicitation, small molecules are defined as organic compounds with a molecular weight of 900 Daltons or less, including nucleotide and nucleoside analogs, that can be chemically synthesized or isolated from natural sources. Concept papers must clearly outline an executable plan to discover/develop an **orally bioavailable, broad spectrum small molecule drug** that targets human pathogens within the Togaviridae and Flaviviridae viral families. Biologics, nucleic acid-based therapeutics, and other non-small-molecule therapeutic modalities are out of scope for the SMART Antiviral Prize.

Formatting Requirements: Text fields are pre-set to Calibri typeface with 1-inch (2.5 cm) margins and 12-point font size; this formatting should be maintained. Images may be included as indicated, with text labeling a minimum 10-point font size.

Criterion 1: Antiviral Target & Rationale

Present a rigorous scientific rationale supported by literature, public datasets, and/or prior work demonstrating the validity of the proposed broad-spectrum antiviral target. Highlight the transformational aspect of the approach and the potential to enhance speed, efficacy and likelihood of success. Evidence supporting this criterion may include in silico, in vitro and in vivo evidence in support.

1. **Target Rationale & Family-level Logic:** Provide compelling evidence that the proposed viral target is appropriate for broad-spectrum small molecule therapeutic intervention. Entrants should justify the choice of target, supported by evidence demonstrating that the target:
 - Is essential for viral entry, replication, and/or persistence;
 - Is conserved across a viral family or families;
 - Has a plausible high barrier to resistance (e.g., conservation, fitness cost, multi-site engagement, etc.); and
 - Is feasibly modulated with a small molecule to produce a desired therapeutic effect (e.g., established precedent, tractability, or binding site rationale).

If the proposed target does not fully meet one or more of these criteria, describe the scientific rationale and key tradeoffs, explaining why the proposed approach remains viable and aligned with program objectives.

1000 words maximum (excluding references)

1 figure maximum

Criterion 2: Development & Regulatory Strategy

Present a detailed and realistic plan for advancing the candidate through key milestones in early-stage development. Highlight the transformational aspect of the approach and the potential to enhance speed, efficacy, and likelihood of success.

2. **In vitro screening approach:** Entrants with early hits identified should summarize the relevant results, how the data were generated, and how the data inform the proposed development strategy. Entrants without existing hits identified should provide a credible *in vitro* screening plan for generating these data. At this stage, screening may use non-live virus approaches (e.g., biochemical/enzymatic assays, binding/biophysics, replicons, pseudotyped virus, or reporter-based assays) to enable higher throughput. Live-virus, cell-based potency testing will be addressed separately in the Stage 1 requirements and/or corresponding application section. Information may include:
- Evidence of access to appropriate chemical libraries, providing verification of stakeholder partnerships if intended libraries are external to entrant.
 - Demonstrated access to relevant assays and reagents.
 - Virus selection and justification, including a comprehensive list of virus species in the screening panel. Include specific strains only when they are critical to the assays/models or known to differ in susceptibility. This should reflect:
 - Relevance to prioritized viral families as outlined in the SMART Antiviral Prize mission and scope, with adherence to the anchor virus requirement.

500 words maximum (excluding references)

1 figure maximum

3. **Developability Assessment Plan for Stage 1: Hit-to-Lead:** Describe the plan to nominate one or more lead series (e.g., a primary and backup series) from distinct structural classes or scaffolds. If only a single lead series is proposed, entrants should provide evidence of chemotype diversity within the series. Please address the following:
- How data will be generated to meet the **Stage 1: Target Compound Profile**, with specific attention to how hits will be confirmed in cell-based, live-virus infection assays to generate EC50 values, including the proposed cell line(s) and clinically relevant virus strain(s)/isolates.
 - Bioanalytical Chemistry (BAC) methods to support accurate and reproducible measurement of the eventual lead(s).
 - Medicinal chemistry plan to support early optimization efforts (e.g., plan to improve potency and selectivity and begin to establish ADME/PK and physicochemical properties.)
 - A conceptual approach for evaluating the potential for antiviral resistance, focusing on strategy and decision criteria rather than specific experimental procedures.
 - A high-level timeline demonstrating how the proposed approach will complete the Hit-to-Lead stage within **18 months** from Concept Stage award, including key technical milestones and critical path activities.

1500 words maximum (excluding references)

1 figure maximum

4. **Development Plan for Lead Optimization and IND-Enabling Efforts:** Describe the anticipated approach to lead optimization and IND-enabling studies, with specific mention of:
- Proposed in vivo challenge models, highlighting the relevance and translational value of the models with specific relevance to the viral target(s) and proposed mechanism(s) of action.

The entrant is encouraged to discuss any proposed partnerships that would yield proof of concept data from adequate challenge models.

- Plans for PK/PD, DMPK, and early safety/POC pharmacology studies appropriate to the stage.
- A high-level CMC strategy to de-risk manufacturability from lead selection through IND-enabling studies, including key assumptions and critical dependencies (e.g., unique starting materials, hazardous chemistries, specialized equipment, constrained suppliers) and intended path to a scalable synthetic route to support preclinical studies and first-in-human readiness, and risk mitigation plan (e.g., alternate suppliers, route back-ups, simplifying structural features).
 - **Detailed routes, specifications, or full stability study designs/data are not expected at the Concept Stage;** however, note any anticipated formulation or stability risks and how they would be addressed as the program matures.
- A high-level timeline demonstrating how the proposed approach will complete the Lead Optimization and IND-Enabling activities within **60 months** from Concept Stage award, including key technical milestones and critical path activities.

500 words maximum (excluding references)

1 figure maximum

5. **Commercialization & Regulatory Strategy:** Include a forward-looking commercialization and regulatory strategy that demonstrates awareness of the regulatory and market landscape. The plan should be updated as the candidate progresses through the SMART Antiviral Prize to align with the published **Desired Product Attributes**, and include:
 - A value proposition to explain what is meaningfully novel about the approach and how it addresses the major shortcomings/limitations of current approaches. Describe the plan to capitalize on this differentiator over time (e.g., development plan, positioning, adoption).
 - The most likely initial indication(s) and explain why those are plausible given the target product goals.
 - Proposed strategy for early regulatory interaction and any relevant guidance the entrant plans to follow, including regulatory mechanisms that could accelerate the review and approval process (e.g. INTERACT meeting, Pre-IND meeting, orphan drug designation, accelerated approval.)

250 words maximum

Criterion 3: Capabilities & Partnerships

Summarize the technical experience, relevant infrastructure, and resources necessary to successfully execute the proposed work. Concept Stage funding is intended to support progression into and through Stage 1; therefore, applicants should prioritize the experience, partnerships, and resources that enable delivery of Stage 1 milestones. However, entrants are encouraged to also describe additional capabilities, partnerships, or past experience that strengthen overall feasibility and efficiency across later preclinical

development (e.g., toward IND readiness), where applicable. Early-stage teams are welcome, provided there is a credible plan and access to the expertise and facilities needed for Stage 1 execution.

6. **Demonstrated Experience and Partnerships:** Include a capability statement that highlights relevant past performance or partnerships. Please emphasize the elements most directly supporting successful Stage 1 execution and include additional strengths that enhance downstream feasibility as appropriate. This may include:
- Evidence that the entrant has successfully conducted similar work in the past relevant to Stage 1 activities (e.g., hit identification/triage, medicinal chemistry, in vitro potency, early DMPK/developability, safety triage).
 - Evidence of any prior regulatory experience with FDA or plans to leverage external regulatory expertise as the program advances, especially as it pertains to antiviral drug development.

500 words maximum

7. **Organizational Capabilities and Resources:** Provide a practical summary of the entrant's internal capabilities, which includes:
- Key personnel already in place; clearly identifying internal staff from external consultants and defining relevant expertise and roles, with emphasis on those needed to deliver Stage 1: Hit-to-Lead milestones (**an organizational chart may be included for this section**).
 - Identification of any gaps in expertise, along with a plan to address them through hiring, training, or anticipated partnerships that enhance the submission's feasibility or efficiency for Stage 1 and beyond.
 - Access to critical technologies, platforms, or facilities required to carry out the proposed work (including those needed for Stage 1).

500 words maximum

1 figure maximum