|  |  |
| --- | --- |
| Principal Investigator: | Draw or paste chemical structure in this space |
| PI Email Address: |
| PI Phone Number: |
| **Submit PI’s NIH Biosketch along with this form** |
| Compound name: |
| Molecular weight (MW): |
| Who will supply compound? | Preclinical model(s) of interest: |
| PI  Purchase from \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | GFAP-Tsc1-CKO epilepsy |
| Check one: | Tsc2+/- A/J renal cystadenoma |
| Clinical Candidate  Mechanistic Tool | Tsc2-null 105K cell xenograft |
| Do you have funding to run this study?\* Y / N | RhebCA epilepsy  Other (specify): |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **DRUG-TARGET RELATIONSHIP** | | | | | |
| **Potency at target *in vitro* (Kd, Ki, etc)** | Untested/ Unknown | >1 μM | 100 nM – 1 μM | 10 nM – 99 nM | <10 nM |
| **Potency at next most sensitive target in same protein class (e.g., kinase, GPCR)** | Untested/ Unknown | >1 μM | 100 nM – 1 μM | 10 nM – 99 nM | <10 nM |
| **Name of next most sensitive target tested for potency:** | | | | | |
| **PRECLINICAL THERAPEUTIC CHARACTERISTICS** | | | | | |
| **Route of administration in animal models** | Untested/ Unknown | Sub-cutaneous minipump | Formulated into chow | IP | Oral gavage |
| **Frequency of dosing in mice** | Untested/ Unknown | Constant (minipump or chow) | Twice daily | Once daily | Less frequently than once daily |
| **Estimated daily dose in mice** | Untested/ Unknown | >100 mg/kg/day | 10-100 mg/kg/day | 1-9 mg/kg/day | <1 mg/kg/day |
| **Maximum tolerated dose in mice or rats** | Untested/ Unknown | <1 mg/kg/day | 1-9 mg/kg/day | 10-100 mg/kg/day | >100 mg/kg/day |
| **Evidence for crossing blood-brain barrier (BBB)** | Untested/ Unknown | Does Not Cross BBB | Limited (<10% of systemic exposure) | Moderate (10-50% of systemic exposure) | Good (>50% of systemic exposure) |
| **Evidence of target engagement using biomarker(s)** | Untested/ Unknown | Not possible to determine | Suggested by PK | Confirmed, but no dose relationship established | Confirmed and dose-dependent |
| **CLINICAL EXPERIENCE** | | | | | |
| **Experience in humans** | Untested | Tested; safety concerns found | Tested; safe in Phase 1 studies | Tested; safe in Phase 2/3 trials | Approved for use by FDA, EMA, or equivalent |
| **If tested in humans, list clinicaltrials.gov identifiers:** | | | | | |

\*Presence or absence of funding (e.g., NIH grant) to support this work does not necessarily impact whether the compound will be tested, but it must be considered for the avoidance of overlapping funding.

Use one or two pages to describe:

* The hypothesis, rationale and specific aims for the compound and its mechanism of action for treating TSC (if available, include evidence to support the hypothesis).
* Compare and contrast proposed mechanism/compound vs. current treatments for TSC. Provide a rationale for differentiation (efficacy and/or safety, other) compared to existing treatments.
* Briefly describe how testing the compound (or a different compound with an identical mechanism of action) in one or more models will be used to move the compound into clinical trials for TSC (provide an outline of next steps for the translation).

If you have any questions, please contact Dean Aguiar, PhD, Director Preclinical Research at [daguiar@tsalliance.org](mailto:daguiar@tsalliance.org).

Delete this instructional text to maximize your use of space.