Compound nomination for testing by the TSC Preclinical Consortium

The Preclinical Consortium Steering Committee (SC) sets the long-term goals, and Working Groups (WGs) decide the best models and experimental design for drug testing and provide oversight for rigorous quality control and interpretation of results. Compounds are handled and tested by experienced contract research organizations (CROs), and data are shared among the Consortium. Any researcher may propose compounds for testing and benefit from the shared data.

For-profit companies interested in nominating compounds and retaining confidentiality and ownership of the data should not utilize the nomination form and should contact Dean Aguiar, PhD, Vice President, Translational Research, directly (daguiar@tscalliance.org).

If you have any technical difficulties with this form, please email Zoë Fuchs, Science Project Manager (zfuchs@tscalliance.org)

Date of Nomination

Principal Investigator (PI) Full Name:
(e.g., Jane Doe, MD, PhD)

PI Email Address

PI Phone Number

Compound Name

Compound CAS Number
About CAS numbers

Compound Molecular Weight

Who will supply the compound?

- ◯ PI
- ◯ Purchase from supplier

Supplier name, web site, and catalog number:

Preclinical model(s) of interest:
Please note that we are only accepting nominations for experimentation in our tumor models of TSC.

- ☐ Tsc2+/- A/J renal cystadenoma
- ☐ Tsc2-null 105k cell xenograft (immune-competent)

What best describes this compound?

- ◯ Clinical candidate
- ◯ Mechanistic tool
- ◯ Other

Do you have funding to run this study?
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.

- ◯ Yes
- ◯ No

What is a measurable mechanistic biomarker that reflects this compound's activity?

How would you propose to measure this compound's target engagement?

Are you willing to run any confirmatory analysis of target engagement with tissues or specimens from the proposed experiment?

DRUG-TARGET RELATIONSHIP

Potency at target

- ◯ Untested/unknown
- ◯ >1 μM
- ◯ 100 nm - 1 μM
- ◯ 10 nM - 99 nM
- ◯ <10 nM

Potency at next-most sensitive target in the 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
- ◯ Intraperitoneal (IP) injection
- ◯ Oral gavage
- ◯ Other [ ]

Frequency of dosing in mice

- ◯ Untested/unknown
- ◯ Constant (minipump or chow)
- ◯ Twice daily
- ◯ Once daily
- ◯ Less frequently than once daily
- ◯ Other [ ]

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

Max 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 the blood-brain barrier (BBB)
Optional for non-CNS experiments

- ◯ 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, please list clinicaltrials.gov/ identifiers:

PROTOCOL-SPECIFIC QUESTIONS

Use one or two pages to describe:

1. 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).

2. 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.

3. 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).

TO SUBMIT

Please upload the following:
1. This PDF form (saved as LastNameForm.PDF)
2. 1-2 page Word or PDF protocol specific questions response document (saved as LastNameProtocol)
3. PI NIH-style Biosketch (saved as LastNameBiosketch.PDF)

Upload to **this secure DropBox link.** If you have any questions or difficulties, please email Zoë Fuchs, Science Project Manager (zfuchs@tscalliance.org)