Draft: June 24, 2021

Public Private Partnership for Preclinical Research in Tuberous Sclerosis Complex
CONSORTIUM OPERATING AGREEMENT

This **CONSORTIUM MEMBER AGREEMENT** ("Consortium Agreement") is entered into as of this_____day of_____, 20___(the "Effective Date") by and between [Name], having its principal place of business at [Address] ("Consortium Member"), and the National Tuberous Sclerosis Association, Inc., d/b/a/ TSC Alliance, having its principal place of business at 8737 Colesville Road, Suite 400, Silver Spring MD 20910 (the "Foundation").

Note: Schemata are provided for visual aid (see end of document). Figures have no legal implications.

I. Mission of the Consortium.

The mission of the Consortium is to accelerate development of therapeutic treatments for tuberous sclerosis complex ("TSC") through the establishment of a collaborative, pre-competitive, international consortium which will provide a forum to combine the expertise and perspectives of stakeholders from industry, academia, governmental agencies and patient organizations to address unmet scientific, technical, clinical and regulatory needs for clinical trials for TSC. Nothing in this Agreement shall authorize the Consortium to undertake activities that are prohibited to be undertaken directly by the Foundation.

II. Consortium Members

(a) **Composition**. The following will be accepted into the Consortium as "Consortium Members:" (i) Companies with interest in TSC who pay the Base Membership Fee ("Company Members"); (ii) Academic Institutions ("Academic Members") with Principal Investigator(s) ("PI(s)") with an ongoing program in TSC research; and (iii) At Large Members who have a unique interest in TSC and are accepted by the Foundation for membership.

(b) **Annual Meetings.** The Consortium will schedule one annual meeting at which speakers will brief Consortium Members on ongoing research and development of TSC therapies and Consortium Members will have the opportunity to meet and discuss current TSC developments. Representatives of government and other patient groups will be invited to the meeting at the discretion of Foundation.

(c) **Company Members Rights and Duties**.

(i) Company Members will be entitled to participation of one representative in quarterly telephonic updates, access to public protocols, raw data, analyses, and interpretation; and

(ii) Company Members will have the right to request compounds to be screened through the Consortium. Compounds will be divided into three buckets as described below:

(A) **Bucket A** compounds are reference (public) compounds of interest to the Consortium. Results from the drug screen will be immediately available to all Consortium Members and may be included in an academic publication produced by the Consortium Members. The identity of the originating Consortium Member will not be released unless the Consortium Member initiating request approves such disclosure in writing. Bucket A studies shall require approval by the Steering Committee. Ownership of any intellectual property shall follow inventorship, as determined by U.S. law.

(B) **Bucket B** compounds are Company Member's (private) compounds of interest to the Consortium. Results from the drug screen conducted by the Consortium will be available to all Consortium Members and available for publication after an escrow period of 180 days after results are communicated to the originating Company Member during which the originating Company Member can seek intellectual property protection of the underlying intellectual property; provided, that, the escrow period can be waived in writing by the originating Company Member or the originating Company Member may extend the escrow period for one additional 180-day period, each by written notice to the Steering Committee. The identity of the originating Company Member will not be released to other Company Members unless such disclosure is approved in writing by the originating Consortium Member. Bucket B studies shall require approval by the Steering Committee.

(C) **Bucket C** compounds are Company Member's (private) compounds of unknown interest to the Consortium. Results from a Bucket C study will not be released to the Consortium Members other than the originating Consortium Member and the identity of the originating Company Member will not be released. Bucket C studies shall not require approval by the Steering Committee and shall have priority over Bucket A studies.

(iii) Company Members who wish to screen compounds as Bucket A or Bucket B should do so using the appropriate Consortium forms (Exhibit A) where it should be indicated which compound is proposed and to which Bucket it belongs. Bucket C compound testing does not require Exhibit A. Company Members are responsible for filing appropriate invention disclosures in advance of the proposal submission.

(iv) Company Members who purchase screening services through the Consortium shall indemnify, defend, and hold harmless the Foundation and its respective personnel and the members of the Working Group and their respective institutions from and against any and all liabilities, damages, losses, claims, or expenses, including court costs and reasonable attorneys' fees, arising out of or in connection with such Company Member's use and/or commercialization of the

results, including any newly created intellectual property, of the aforementioned screenings whether by or through Company Member.

(e) Academic Members Rights and Duties.

(i) The Foundation will appoint Academic Members and may issue calls for proposals to help identify Academic Institutions eligible to be Academic Members.

(ii) PIs of Academic Members may participate in quarterly telephonic updates, receive access to public protocols, raw data, analyses, and interpretation.

(iii) Academic Members who wish to have compounds screened through the Consortium can propose to do so using the Submission Forms ((Exhibit A) with the consent of the Secretariat as follows:

(A) **Bucket A** compounds are reference (public) compounds of interest to the Consortium. Results from the drug screen will be immediately available to all Consortium Members and may be included in an academic publication produced by the Consortium Members. These studies require approval by the Steering Committee. Ownership of any intellectual property shall follow inventorship, as determined by U.S. law.

(B) **Bucket B** compounds are the Academic member or its Academic Institution (private) compounds of interest to the Consortium. Results from the drug screen will be available to all Consortium Members and available for publication after an escrow period of 180 days during which the Academic Member may obtain intellectual property protection; provided, that, the escrow period can be waived by the originating Academic Member or the escrow period may be extended for one additional 180-day period, each by written notice from the Academic Member to the Foundation. These studies require approval by the Steering Committee.

(iv) PIs of Academic Members who wish to have compounds screened through the Consortium should do so using the appropriate Consortium forms where it should be indicated which compound is proposed and to which Bucket it belongs. PIs are responsible for filing appropriate invention disclosures with their corresponding Academic Members in advance of the proposal submission.

(f) At Large Member Rights. The Foundation may accept other members who have an interest in Consortium activities as At Large Members. The cost of membership and other conditions of At Large membership shall be determined by the Foundation. For example, Screening Centers (whether for-profit or not-for profit entities) approved by the Foundation may be At Large Members.

At Large Members shall be entitled to the following:

(i) Access to public protocols, raw data, analyses, and interpretations;

(ii) Participation in the Annual Meeting; AND

(iii) Updates following each Steering Committee meeting.

(g) Consortium Membership and Screening Fees.

Class of Member	Base Membership Annual Fee	Bucket A Screening Fee	Bucket B Screening Fee	Bucket C Screening Fee
Company	**$25,000 in 2021**	**20% cost of screening***	**75% cost of screening***	**100% cost of screening***
Academic	**-**	**-**	**20% cost of study**	**N/A**

***Cost of screening includes any royalty owed for tools or models required, such as licensing fees for the animal models, and a 10% overhead for the Foundation's support.**

(h) Novel Compounds. In the event a novel compound not covered in Buckets A, B or C above is deemed of interest to the Consortium, the Secretariat, with the recommendations of the Steering Committee, will determine on a case-by-case basis whether any such compound shall be screened through the Consortium. Any invention resulting from Consortium-funded research using such compound may be patented by the Consortium and licensed on a non-exclusive basis to Consortium Members on terms and conditions to be determined by the Foundation. The Foundation may also decide if such invention will be licensed to third parties on a royalty-free basis or whether charging a royalty to certain licensees may best serve the charitable interests of the Foundation.

III. Steering Committee.

(a) **Designation.** The members of the Steering Committee ("SC Members") shall be selected (and may be removed for good cause) by Foundation, taking into account the recommendations of the current members of the Steering Committee.

(b) **Steering Committee Membership.** The voting members of the Steering Committee shall consist of no fewer than six (6) and no more than twelve (12) persons divided into the following categories: (i) approximately one-third of the voting members of the Steering Committee shall be representatives of Company Members that are actively engaging in development of therapies for the treatment of TSC or planning to undertake such development efforts in the future (the "Company SC Members"); (ii) approximately one-third of the voting members shall be Academic Members (the "Academic SC Members") and (iii) the remaining approximate one-third shall be representatives of the Foundation, TSC patient community or other patient organizations. The Consortium Director, who

shall be solely designated by the Foundation, will be a voting member of the Steering Committee and shall serve without term limitation.

(c) **Chairpersons.** The Foundation shall designate two (2) SC Members from any of the Steering Committee membership categories specified in subparagraph (a) (but not more than one (1) from each category), to serve as co-Chairpersons of the Steering Committee. The Chairpersons shall preside over all meetings of the Steering Committee and approve the agenda proposed by the Foundation in advance of each meeting before it is circulated to the SC Members.

(d) **Term.** The term of each SC Member shall be two (2) years, or if such SC Member is replacing an SC Member for his or her unexpired term, for the remainder of such term. Prior to the expiration of the term, the Foundation may request that the SC Member serve an additional term, provided that the term of any SC Member shall be limited to three (3) two-year consecutive terms. During the first year of this Consortium half the SC Members, chosen at random, will have 3-year terms to ensure renewal in a staggered manner.

(e) **Meetings.** The Steering Committee shall conduct a face-to-face meeting at least twice per year. The second face-to-face meeting shall be referred to hereinafter as the "Fall Meeting," provided that if more than half of the SC Members cannot attend a Steering Committee meeting in a given year, the meeting can be held by conference call. In addition, the Steering Committee shall meet by telephone or other means by which each of the SC Members can hear the remarks of the other SC Members. The Fall Meeting shall be held prior to the time the Company Members are formulating their budgets, so that they can account for and consider their contributions to the Consortium given the progress achieved during the year and or the projects the Consortium is proposing to prioritize for the following year.

(f) **Attendance**. SC Members are strongly encouraged to attend each meeting of the Steering Committee. While it is recognized that business and personal reasons may prevent attendance at meetings from time to time, the failure to attend two or more consecutive meeting may constitute good cause for removal. If an SC Member is unable to attend a meeting, he or she may designate a substitute from the organization he or she represents, who can represent the absent SC Member's views, provided that the substitute's attendance at a Consortium's meeting shall not constitute attendance for purposes of the preceding sentence.

(g) **Purpose of the Steering Committee.** The Steering Committee shall perform the following functions:

(i) Adopt this Agreement and subsequently recommend amendments;
(ii) Develop an overarching plan to guide drug screening efforts;
(iii) Establish priorities, strategic direction, and deliverables;

(iv) Vote on and oversee the Consortium budget, status of collaborative efforts and Working Groups, and changes in direction and funding for the Consortium; and

(i) Establish procedures and policies to be followed by the Consortium.

(h) **Voting.** The vote of the Steering Committee shall be to provide recommendations to the Foundation and such recommendations shall be taken into account in determining the budget, activities and policies of the Consortium. Voting shall be conducted at meetings only when a quorum of the SC Members is present. The presence of a majority of the SC Members, including the Consortium Director, shall constitute a quorum, provided that at least one (1) SC Member from each membership category is present at the meeting. Votes by a majority of the SC Members present at a meeting at which there is quorum shall be communicated to the Foundation by the Secretariat.

(i) **Conflicts of Interest.** A conflict of interest may exist when the interests or concerns of a SC Member or the organization he or she represents compete with the interests or concerns of the Consortium. Any possible conflict of interest shall be disclosed to the Consortium by an SC Member. When any such conflict of interest is relevant to a matter on which the Consortium is considering taking action, the interested SC Member shall retire from the meeting, shall not participate in the final deliberation of the matter, and shall not vote on the matter. The minutes of the Steering Committee shall reflect the conflict disclosure and that the interested SC Member was not present during the final deliberation and vote and did not vote on the matter. When there is a doubt as to whether a conflict of interest exists, the matter shall be resolved by a vote of the Steering Committee. If appropriate, the Steering Committee shall seek the advice of legal counsel on whether a conflict exists and on the nature or the potential effect of any such conflict.

(j) **Advisory Members.** The Steering Committee shall, when it determines it to be appropriate, appoint advisory members of the Steering Committee. Without limitation, the advisory members may possess special expertise on a matter of concern to the Consortium, regulatory concerns, or represent particular geographic locations or patient groups. The advisory members shall serve for such period requested by the Steering Committee, shall have no vote but may be requested to attend meetings of the Steering Committee when their attendance will assist the Steering Committee in considering particular issues.

IV. Secretariat.

(a) **Composition.** The Secretariat of the Consortium shall be the personnel assigned by the Foundation to staff the work of the Consortium. One of them shall serve as the Consortium Director.

(b) **Duties and Responsibilities**. The Secretariat shall perform the following duties:

(i) Provide operational and strategic leadership to the Consortium;
(ii) Plan, coordinate and oversee all activities related to the Consortium;
(iii) Report to the Steering Committee on the progress of the Working Groups;
(iv) Ensure communication between all Consortium Members;
(v) Act as the liaison between Steering Committee, Working Groups, advisory members, Members at Large, and external partners;
(vi) Enforce project milestones;
(vii) Propose the membership of the Working Groups to perform the projects recommended by the Steering Committee and approved by the Foundation;
(vii) Review proposals for projects and prioritize them for submission to the Steering Committee and to the Foundation for approval;
(viii) Propose the Consortium annual budget to the Steering Committee for its recommendations;
(ix) Provide administrative support for the Consortium, the Steering Committee and the Working Groups;
(x) Organize all meetings of the Steering Committee, provide notices to the Members of the time, location and agenda of the meetings of the Steering Committee and following each meeting promptly prepare and circulate minutes of the meeting;
(xi) Organize all meetings and coordinate Consortium Working Groups and obtain reports from the Working Groups to be circulated to the Steering Committee and Foundation; and
(xii) Undertake all other duties assigned to it by the Steering Committee.

V. Working Groups.

(a) **Purpose**. Much of the work of the Consortium will be conducted through Working Groups on projects recommended by the Working Groups recommended by the Steering Committee and approved by the Foundation. The Working Groups will design and implement projects or programs in collaboration with the Foundation.

(b) **Composition.** The Working Groups generally will be composed of academic researchers and certain other experts who have been selected by Foundation because of their unique expertise, have volunteered, and have experience with TSC. The composition of the Working Groups will be proposed by the Foundation,

(c) **Meetings.** The Working Groups will meet with the Consortium Director or another member of the Secretariat monthly and provide periodic progress reports semi-annually or more frequently at the request of the Consortium Director.

(d) **Types**. There will be two initial Working Groups, the Pathology Outcomes and the Functional Outcomes Working Groups. If necessary, the Steering Committee can change the structure and function of the Working Groups.

(e) **Project Planning**. The Working Groups shall be responsible for reviewing compound screening requests and designing the screening studies that shall be carried out by third-party labs.

(f) **Analysis**. The Working Groups shall be responsible for analyzing the data generated by the screening studies and coordinating any publication of such data.

VI. Sharing of Data and Results.

Consistent with its purpose to accelerate research of new TSC therapies, the Consortium will accumulate certain data and results from Bucket A and Bucket B projects undertaken by the Consortium and the Working Groups (collectively, the "Results"). Subject to delays that may be necessary to obtain intellectual property protection on any inventions contained in the Results and customary publication delays, the Consortium intends to distribute the Results to relevant academic researchers, Company Members, and eventually to the general interested public. Consistent with this intent and subject to the terms of this Agreement, the Consortium will respond to all relevant requests to distribute such Results, and place the raw data, analysis, and interpretation of Results in an open access forum.

VII. Confidentiality.

As set forth in Article VI, the Consortium shall distribute broadly the Results of the Consortium's work to researchers and companies developing TSC therapies. Accordingly, the Results will be made available to the general public and will not be confidential. Nevertheless, there are aspects of the Consortium's work that by necessity must be confidential, such as the internal deliberations of the Steering Committee that will lead to choosing its priorities, its budget and sources of funding, and potentially other matters for which third parties impose a duty of confidentiality. Accordingly, Working Group members and experts will be asked to execute an appropriate non-disclosure agreement and will be held to standards similar to those imposed on directors of charitable organizations.

VIII. Compensation.

No Working Group member or SC Member shall receive compensation solely for participating in the Working Group or Steering Committee. However, any Consortium Member may be reimbursed for his or her actual expenses incurred in the performance of duties on behalf of the Consortium. For clarity, a Working Group Member may be separately asked to perform services for the Consortium. Such services will not be considered to be solely for participating in the Working Group and may be compensated.

IX. Consortium Budget and Funding.

(a) **Budget**. Each year no later than September 1, the Foundation shall propose the Consortium budget for the following year for consideration by the Steering Committee. The budget shall include anticipated expenses and revenues, including the direct expenses of the Secretariat.

(b) **Other Funding**. It is anticipated that an important portion of the funding of the Consortium will be provided by the Foundation and bio/pharma companies that recognize the need to develop new therapies for TSC patients. However, the Secretariat will seek to obtain revenue commitments from other SC Members, outside partners, and government and Foundation grants, and other sources to cover the full expenses of the budget. The Secretariat will report on to the Steering Committee on the progress of its fundraising efforts at the Fall Meeting.

X. Funds Administration.

The Foundation, in good faith, shall:

(a) Maintain charge and custody over all Consortium funds, which shall be accounted for separately on the books and records of the Foundation;

(b) Be responsible for maintaining accurate, properly stored and up-to-date records of all Consortium transactions;

(c) Deposit and administer all funds of the Consortium; and

(d) Provide the Steering Committee with an annual financial report.

XI. General Policies and Procedures.

The Consortium shall develop policies and procedures consistent with this Agreement that are intended to create a trusted and collaborative environment to facilitate exchange and development efforts by the Consortium while ensuring compliance with relevant requirements of applicable law.

XII. Contracts with Screening Centers

The Foundation shall have the right to enter into contracts on behalf of the Consortium with one or more third parties who shall provide compound screening services to the Consortium ("Screening Centers"). Such contracts shall at all times be subject to and consistent with this Agreement.

XIII. Duration.

The Consortium will continue to exist until Foundation makes a determination that the Consortium no longer serves the mission identified in this Agreement.

XIV. Amendment of this Agreement.

This Agreement may be amended by the Foundation after considering the recommendations of the Steering Committee.

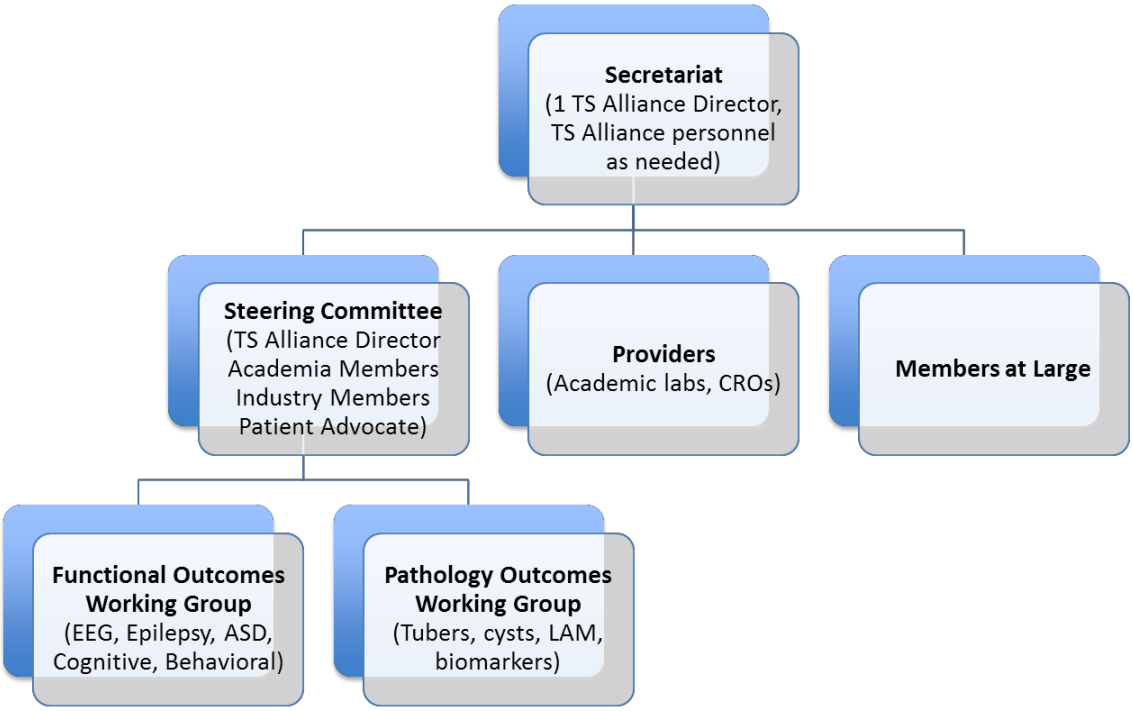
XIV. Miscellaneous.

(a) The person signing below on behalf of a Consortium Member represents that he or she has the full power and authority to enter into this Consortium Agreement on behalf of such Consortium Member.

IN WITNESS WHEREOF, the parties hereto, each by a duly authorized representative, have executed this Consortium Agreement as of the date first written above.

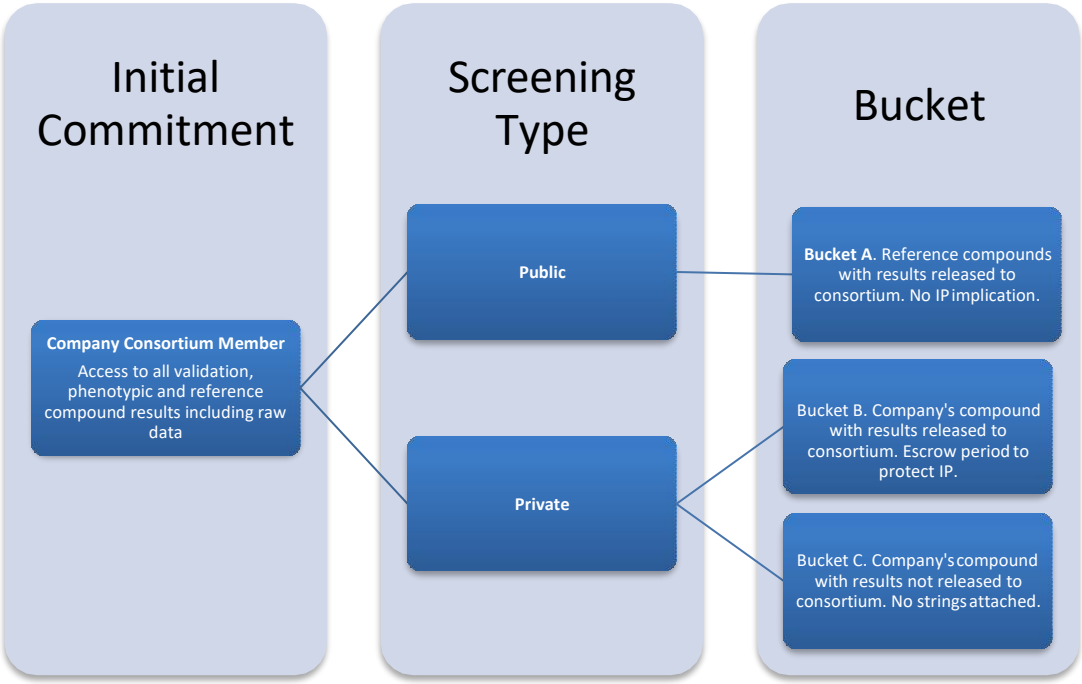
[NAME of Consortium Member**]**	**TSC Alliance**
By:_____	By:_____
Authorized Signature	Authorized Signature
Name:_____	Name: Kari Luther Rosbeck
Title:_____	Title: President and CEO
Date:_____	Date:_____

SCHEMA I


Secretariat
(1 TS Alliance Director, TS Alliance personnel as needed)
Steering Committee
(TS Alliance Director
Academia Members
Industry Members
Patient Advocate)
Providers
(Academic labs, CROs)
Members at Large
Functional Outcomes Working Group
(EEG, Epilepsy, ASD, Cognitive, Behavioral)
Pathology Outcomes Working Group
(Tubers, cysts, LAM, biomarkers)

SCHEMA II – Types of Membership

1. Industry Membership



2. Academic Membership

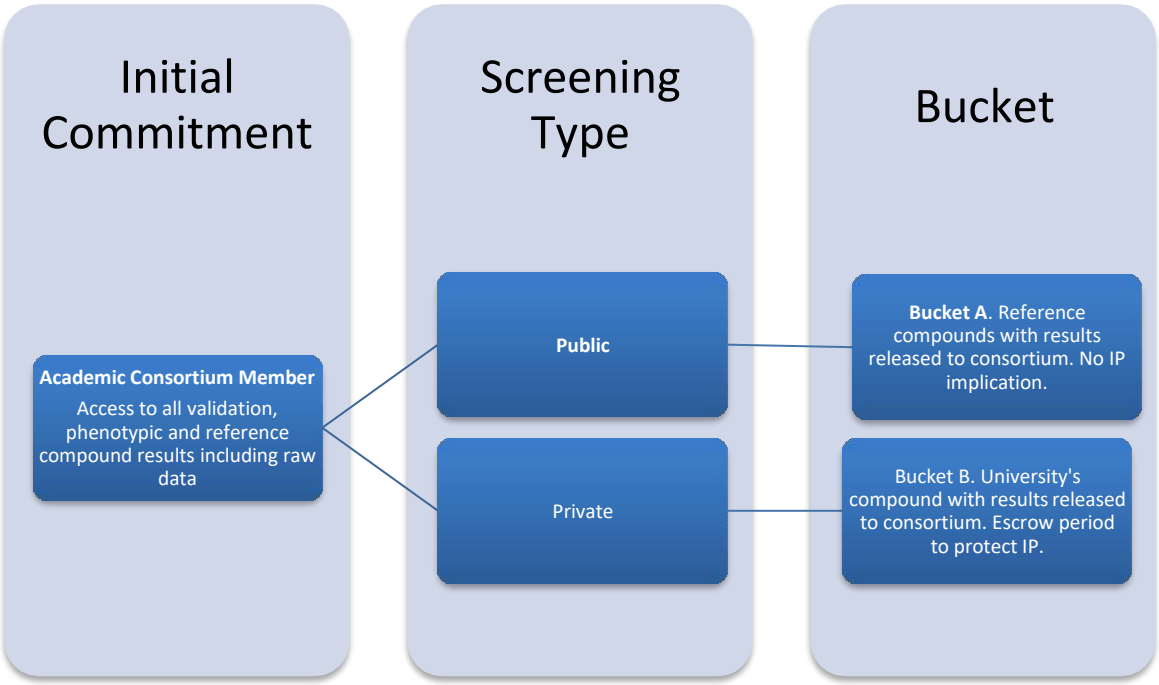


Exhibit A – Submission Form

Principal Investigator: Institution: PI Email Address: PI Phone Number: Compound name: Molecular weight (MW): MW of salt form, if applicable: Check one: ☐ Clinical Candidate ☐ Mechanistic Tool	Draw or paste chemical structure in this space Preclinical model(s) of interest: ☐ GFAP-Tsc1-CKO epilepsy ☐ $Tsc2^{+/-}$ A/J renal cystadenoma ☐ Tsc2-null 105K cell xenograft ☐ Other (specify):

DRUG-TARGET RELATIONSHIP					
Potency at target *in vitro* (K_d, K_i, 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:					

Use one page to describe a rationale for the compound and its mechanism of action for treating TSC. Include the rationale for how this mechanism of action or this specific compound could be superior to existing treatments. Include a brief description of how testing this compound in one or more models within the Preclinical Consortium will be used to move the compound (or a different compound with an identical mechanism of action) into clinical trials for TSC. You may delete this instructional text to maximize your use of space.