Autism Speaks Request for Applications
2018 Treatment Research Grants

Submission, Review & Notification Schedule (subject to change):

Letter of intent due:	July 18, 2018, 8 pm Eastern Time
Letter of intent notifications:	Early August
Application due:	**September 19, 2018, 8 pm Eastern Time**
Peer review panels:	October/November 2018
Notifications:	Late December 2018
Earliest grant start date:	February 2019

I. Introduction

Autism Speaks invites Treatment Research Grant applications to conduct *innovative* studies of novel treatments and interventions for people with autism spectrum disorder (ASD) throughout the life span. These may include medical approaches such as pharmacological treatments and complementary and alternative forms of health care, as well as behavioral and/or psychosocial interventions. Successful applications will focus on evaluation of the efficacy, effectiveness or other therapeutic benefits of the targeted intervention.

The Treatment Research Grant award mechanism directly addresses Goal #3 in our Autism Speaks Science Strategic Plan for 2018-2020: Facilitate the clinical testing of promising life-enhancing interventions. Specifically, this mechanism focuses on efficacy or comparative effectiveness research using rigorous methodologies. The expectation is that funded investigations will produce evidence that guides future practice or key results that motivate future large-scale investigations. Safety and cost-effectiveness can, and often should, be included elements but should not be the sole or primary focus of the study. Open-label or purely observational studies are not recommended. Animal model pre-clinical studies will not be considered for this mechanism.

II. Awards

We anticipate making two awards at $250,000/year for three years with a maximum of $750,000 per award, inclusive of indirect costs.

An amount not to exceed 10% (inclusive) of direct costs may be used for the sponsoring institution's indirect (overhead) costs. The annual maximum $250,000 must include the 10% indirect costs.

Successful applications will include consideration of one or more of the following priorities in the aims, design and/or implementation of the study:

1. Inclusion of cognitively impaired individuals with ASD.

2. Inclusion of validation sensitive, objective, quantitative outcome measures and/or biomarkers as secondary outcomes that can be measured longitudinally.

3. Focus on one or more of the common, co-occurring medical or behavioral conditions that reduce quality of life in autism – either as a primary or secondary outcome measure (in addition to core autism symptoms).

4. Focus on an intervention with potential to improve the transition to adulthood and/or the health and well-being of adults with ASD.

Note: Successful applications are not expected to include all elements.

Additionally, Treatment Research Grants *must satisfy the following requirements:*

- Build on existing feasibility, safety and/or efficacy data to further investigate biomedical or behavioral treatment approaches.
- Be supported by promising results in previous research, by a body of existing research evidence and/or by a strong theoretical justification.
- Come from established investigators with demonstrated potential for and a commitment to biomedical research in autism or related developmental disabilities.

Study design should include consideration of methodological features that influence the risk of bias and confidence in study inferences – including adequate recruitment and retention procedures, randomization, allocation and blinding of treatment (where possible) and outcome assessments. Applicants must demonstrate adherence to recommended practices for ensuring privacy and confidentiality of subjects throughout the process of outreach and recruitment, data collection and data analysis. Applicants must also provide an assessment of benefits versus risk of proposed treatment or therapeutic approach for the target population. Applicants should also consider the ICH Efficacy Guidelines, especially those pertaining to Statistical Principles for Clinical Trials (E9 and E9 (R1)).

See also the Cochrane Collaborative Risk of Bias Tool for more information.

Inclusion of procedures for sample-size estimation and related power analyses is required, with clear explanation of the model and assumptions chosen to estimate statistical power, sufficient power to detect clinically meaningful effects, justification of the chosen effect size and adequate reserve power for secondary outcomes. It is important that applicants clarify if the study is sufficiently powered for addressing the primary objective, secondary efficacy/effectiveness objectives and secondary objectives related to safety, tolerability and adverse effects.

Statistical analyses must align with the chosen design of the trial and should be conducted according to recommended best practices for clinical trials and related intervention studies and include models that are truly intent-to-treat. Please consider recent guidance on statistical analysis plans in proposal development.

Appropriate data collection, management and data handling strategies must be included to ensure privacy and confidentiality of subjects. Trial conduct considerations including data safety and monitoring, interim analysis and early stopping, sample size adjustments as well as accrual rates must be described to ensure sufficient quality and integrity in trial data collection, handling and analytical procedures.

Investigations must be registered with clinicaltrials.gov. Data sharing with the National Database for Autism Research (NDAR), as applicable, is strongly recommended upon study completion. Public pre-registration of the statistical analysis plan, research protocol and upload of final de-identified data to a repository following study completion are recommended.

III. Eligibility

Investigators holding full-time faculty appointments, professional affiliations or equivalent at accredited academic, medical, research or educational institutions are eligible to apply. Postdoctoral fellows who have a strong team and can show proof of a full-time faculty appointment by the expected grant start, are also eligible. Applications will NOT be accepted from individuals or proprietary organizations to support the research and development of products or treatments for profit. Principal Investigator or Co-Investigator applicants are restricted to one submission per RFA. *Multiple submissions will be withdrawn.*

IV. General Instructions

All applications must be submitted through the online Autism Speaks Science Grants System.

Please Note:

1. The Principal Investigator must be the applicant. Go to https://science.grants.autismspeaks.org and register with your **institutional** email address (or log in if you have an ID). We recommend using the following browsers: Chrome, Firefox or IE 10 or higher. Complete your profile information.
2. ORCID profiles – Autism Speaks policy requires all applicants and co-investigators to obtain ORCID profiles and link them to their Autism Speaks Grant System profile. *Link to Help document*. Applicants will not be able to work on their application until they have connected their ORCID profile to their Autism Speaks profile. Links in the Autism Speaks Science Grant system will make this step easy.
3. It is advisable to review the LOI page and then the Application page in the grant system well in advance of any submission date.
4. Uploaded documents should be 11-point Arial font with 1-inch margins all around; single spacing is acceptable. NIH Biosketches can be submitted with their default margins and fonts. Please do not have headers or footers (including page numbers) in submitted documents. Applications exceeding the specified document limits will not be reviewed.
5. Preferred file type is PDF and must not be encrypted. Movie files are not acceptable.
6. It is the applicant's responsibility to contact their Office of Sponsored Projects (or the equivalent) to identify the Responsible Official (RO) for this application. The Responsible Official will review and submit the final portion of the application. Their submission is their approval of the application on behalf of the institution. LOI forms can be completed and submitted by the applicant. Full applications can only be submitted by the RO. The RO's name and contact information will be a part of the LOI page.

VI. Completing the Letter of Intent (LOI)

Log in and click "Applications" at the top of the profile page or "Go to Applications" at the bottom of the page. Choose "Start a new LOI or application" then "Treatment 2018". The LOI includes two web pages, the Basic Information Page and the LOI Form. The requirements for each page are as follows:

1. Basic Information Page includes:
   a. **Title**: Enter less than 100 characters, spaces included.

b. **Scientific Abstract**: (up to 2,000 characters, spaces included) that describes the project goal(s) and/or hypothesis, specific aims, research methods, expected results and significance/relevance to the goals of this RFA.
c. **Brain Tissue Sources**: Complete as applicable to the research project.
d. **Co-Investigators and Collaborators** (tip: start by entering the last name). It is important to enter all individuals participating in the research project. Final changes to this field will be made during completion of the application.
e. **Responsible Official**: Choose the Responsible Official from the PI's institution. You must have an institutional email to add a new person.
f. **Keywords**: Carefully select all the relevant keywords associated with the research project. This information is used to select expert reviewers who are knowledgeable about your particular field of study.
g. Note: **All this information will be available for review and editing at the application stage.**

2. Letter of Intent Form includes:
   a. **Autism Speaks' priorities**: Select one or more of the 4 priorities described above (inclusion of cognitively impaired individuals, objective measures, co-occurring conditions and adult transition and outcomes).
   b. **Priority Explanation**: Explain how the priority or priorities selected above will be addressed by the research project. (up to 2,000 characters, spaces included).
   c. **Principal Investigator Biosketch:** NIH format not to exceed 5 pages.
   d. **Letter of Intent Narrative**: Not to exceed two pages, and must include:
      i. A concise description of the proposed project including brief background/study justification, specific aims, methods, expected results and potential impact on autism.
      ii. Justification for the relevance and potential significance of the project to one or more of the priority research areas described above.
      iii. Any references must be included in the 2 pages.
      iv. The LOI should be specific enough to be screened for scientific merit, fidelity to the purpose of this RFA and relevance to Autism Speaks' priorities.
   e. **Letter of Eligibility**: A letter, one page maximum, from the institution's Office of Sponsored Projects (or its equivalent) or the Head of the PI's department/school/division, confirming the PI's eligibility. Please refer to section III above.

IMPORTANT NOTE: LOIs will be subject to in-depth review. After all LOIs are reviewed, Autism Speaks will send an email indicating approval or disapproval. *Please do not contact the grants staff regarding LOI acceptability.* Applicants with approved LOIs will be permitted to submit a full application. All decisions are final.

VII. Completing Your Application

If you are notified that your LOI has been approved, you will be able to begin your application. Log in and select your application.

1. ORCID profiles **– Autism Speaks policy requires all applicants to obtain ORCID profiles and link them to the Autism Speaks Grant System profile.** Link to Help document**. See General Instructions for details.**
2. **Basic Information Page**: Review and edit your entries from the LOI.
3. **Research Plan:** (6-pages maximum) the research plan should address the evaluation criteria in section IX below.

a. **Background and rationale** for the study. Briefly describe the primary motivations and prior research; no need to reference basic information about ASD.
b. **Research strategy**, including specific aims, participant exclusion/inclusion criteria, recruitment strategy and feasibility, preliminary data, methods and procedures, statistical power, and statistical analyses to address specific aims. Information on study timeline, medication/intervention availability (where applicable), path to dissemination, clinical implementation, and/or future validation/regulatory approval steps. Potential pitfalls and proposed solutions should also be listed.
c. **Innovation.** Describe how the project is novel, ground-breaking and has the potential to move the field in new directions.
d. **Impact** in terms of potential to improve the lives of persons with ASD.
e. **Investigators' Qualifications.** Briefly describe (Biosketches must be provided; see J below)
f. **Environment.** Briefly describe, with greater detail included in H, described below.

4. **Figures**: If needed, include a maximum of two pages of relevant images, figures and graphics. Images uploaded here will not be counted toward the 6-page limit.
5. **Bibliography**: Include complete literature citations including titles and all authors. References will not be counted toward the 6-page limit.
6. **Budget table: Complete the online budget table (in USD, no decimals). The budget may include:**
    a. **Personnel Costs (not to exceed the percent effort committed to the proposed project) FTE salary cap is $189,600 USD.**
        i. **Principal investigator and/or Co-Investigator salaries and benefits**
        ii. **Technical research assistant salary and benefits**
        iii. **Research assistant or fellow stipends and benefits are allowed. (NOTE: Tuition reimbursement is not allowed.)**
        iv. **Consultants**
    b. **Research supplies, services and related expenses**
    c. **Essential equipment. A vendor estimate is required for a single item of equipment costing more than $5,000 US.**
    d. **Travel to professional meetings**
    e. **Publication and data analysis costs**
    f. **Indirect costs: An amount not to exceed 10% of direct costs may be included for the sponsoring institution's indirect (overhead) costs. The total grant cannot exceed $250,000 USD.**
    g. **Collaborations: If you are collaborating with other sites, put their total amount in a "subcontract" row (one row for each site) and include an appropriate explanation in the budget justification section. Total indirect costs for both sites cannot exceed the maximum allowed.**
7. **Budget justification** (4 pages max) the budget justification should provide an explanation for all lines in the budget for all years.
8. **Human participants**: Applications that use human participants must address issues of protections. If no ethics approval is needed for the proposed research, please upload a

memo to that effect. Note that ethical approvals from the applicant organization are required before a grant can be started. These approvals do not serve in lieu of the information requested below.

a. HUMAN PARTICIPANTS (defined as living individuals)
    i. Scientifically justify the involvement of human participants in the proposed research.
    ii. Describe in detail the plan for the involvement of human participants in the proposed research.
    iii. Describe in detail the potential risks to participants and measures to be taken to protect participants from those research risks.
    iv. For clinical trials, describe plans for data and safety monitoring, including the description of a data and safety monitoring board if necessary.

9. **Resources and research environment**: (1-page max) Describe the resources and environment that will support the successful completion of the project. If the project will use existing samples and/or collecting samples, specify how and when they will be used and shared with the autism community following the end of the project.
10. **Letters of Collaboration**: If needed in support of the research project, combine multiple letters into one file for upload.
11. **Biographical sketches**: For the principal investigator, named co-investigators and collaborators in NIH format (5 pages max each). Indicate education, personal statement, positions and honors, contribution to science with relevant citations, selected list of published work, and ongoing and completed research support with emphasis on projects relevant to the proposed investigation. Combine multiple biosketches of co-investigators and collaborators into one file for upload.
12. **Current and pending grant support**: Indicate funding source, total award amount, award duration (inclusive dates) and project title for all investigators and significant collaborators. Financial and substantive overlap will be examined after review.
13. **Supporting files:** Reference other documents relevant to the application in the research plan and upload to "Additional Materials." Combine multiple documents into one file for upload.
14. **Peer-reviewed research publications**: A maximum of two (including manuscripts accepted for publication) will be accepted, but NOT manuscripts not yet accepted for review, review articles, book chapters, popular press articles or meeting abstracts. Publication files MUST NOT be locked or protected in any way.

NOTE: *Supporting files, publications and updates (see VIII) are provided as a courtesy to the reviewers who are not obligated to refer to them in evaluating an application.*

VIII. Endorsing & Submitting the Application

Applications must be submitted electronically using the Autism Speaks Science Grants System. Applications that are late, incomplete, exceed the document limitations or do not adhere to the required format will not be reviewed. Applications that are faxed or emailed will not be reviewed.

When an LOI is approved, the Responsible Official named in the LOI will be copied on the notification email. When the application is ready, it is the responsibility of the applicant to contact their Responsible Official, who must complete the submission. The Responsible Official's submission of the application signifies endorsement on behalf of the institution.

Autism Speaks reserves the right to return without review any application that in its judgment is not in compliance with its rules and procedures for application preparation and submission, is not responsive to its research goals or exceeds its funding limits or available resources. It is the responsibility of the applicant to ensure that the application is complete and conforms to the guidelines.

IX. Review Process and Evaluation Criteria

Autism Speaks is committed to efficient, fair and expert review and funding of meritorious applications that are relevant to the mission of Autism Speaks. Review of scientific merit is provided by a group of highly accomplished researchers from the Autism Speaks Medical and Science Advisory Board with additional expertise, as needed, from other researchers in the specific research areas of the applications.

Applications are evaluated using the following criteria:

Rationale

Is there a solid scientific rationale for the choice of intervention? Is there evidence of safety, efficacy and/or effectiveness in related conditions or does the existing evidence suggest target engagement relevant to autism?

Impact and Relevance

Will the proposed research and expected results contribute new knowledge or methods to improve the lives of people with autism spectrum disorder or their families? Does the application directly address the Autism Speaks' targeted priority areas as described above? To what extent do the aims and hypotheses have the potential to move the field forward?

Innovation

Does the application develop innovative and creative approaches to intervention? Does the project propose to develop or employ novel concepts, approaches or methodologies, tools, or technologies for this area? Does the application challenge an existing paradigm or practice? Will the project application propose ideas or methods that have not been previously used in autism research or have not been applied in the way that is proposed?

Research Strategy

Is the project proposed well designed? Is there preliminary data to establish feasibility and support the likelihood of further success? Are the key components of the sample, methods and data analytic approaches well described and reasonable? Does the proposed design, sampling and analytical methods align with the study hypotheses? Does the application present well-reasoned, realistic and appropriate to the strategy, milestones and timeline of the proposed project? Are potential problem areas acknowledged, alternative tactics considered, and benchmarks for success presented? Will the required methods and analyses be available and implemented appropriately, and are they feasible for this research team relative to the scope of the proposed project? Is the timeline reasonable? Are approaches to disseminate research results or next steps in validation/regulatory approval specified and realistic?

Investigators' Qualifications

Do the investigators have the appropriate training and expertise to conduct the proposed research? Does the investigative team have experience working together? Have they demonstrated satisfactory productivity, relative to stage of career, in terms of peer-reviewed publications and other benchmarks relevant to the proposed research? Have the necessary collaborations been established and documented with letters of agreement?

Environment
Do the performance sites where the work will be done contribute to the probability of success? Is the scientific environment conducive to the work proposed, in terms of institutional support, physical resources and clinical and intellectual resources? Will the proposed studies benefit from unique features of the scientific environment, subject populations or collaborative arrangements? Has access to necessary special research equipment, data bases and/or facilities been appropriately documented with letters of agreement? Does the application document access to the appropriate clinical/laboratory resources needed to conduct the proposed study?

X. Public Access/Dissemination/Attribution:

Acknowledgement: Grant recipients must acknowledge Autism Speaks (including grant#) on all publications and presentations based, in whole or in part, on data derived from the funded research. In addition, you should cite Autism Speaks support in any publicity or communication (internal or external) about the funded project. This includes press releases, media reports, interviews and oral or poster preview of data.

Public Access: Autism Speaks has adopted a public access policy for all Autism Speaks funded research. Grantees are required to retain copyright on their manuscript submissions and ensure deposit in PubMed Central so they are made publicly available no later than 12 months after initial publication. This requirement applies to all grants awarded after December 3, 2008, whether Autism Speaks funds the research in whole or in part. Public Access Policy link

Autism Speaks reserves the right to make information about funded grants publicly available. Funded research projects may be subject to data and resource sharing requirements.

XI. Miscellaneous

Human Subjects Certifications must be documented with a copy of an official letter of approval (or equivalent for non-US applicants) that identifies the Principal Investigator, project title and date of approval, and is signed by the Review Committee Chair or equivalent responsible institutional/government official. Prior certification for another project cannot be substituted, but can be officially amended to include the proposed project (identified by project title and Autism Speaks grant ID# for the project).

IMPORTANT: IRB (or equivalent ethical) certification is NOT required to submit an application; however, IRB (or equivalent ethical) certification must be submitted as soon as possible following official notification of an award. Autism Speaks will NOT issue any payment of a grant until this certification is received.

The first payment will be contingent upon receipt of the countersigned grant agreement letter and certification of ethics approval, if applicable. Subsequent payments are dependent on reports submitted to the online Autism Speaks Science Grants System.

XII. Contacts:

Grants Administration/Online Application/Budget Questions:

Joan New, MBA, Grants Manager: 609-228-7313; jnew@autismspeaks.org

Application Development:

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