



## Strategic Plan for Science 2018 – 2020

### **OVERVIEW**

#### *Autism Speaks Mission*

Autism Speaks is dedicated to promoting solutions, across the spectrum and throughout the lifespan, to meet the needs of individuals with autism and their families. We do this through advocacy and support; increasing understanding and acceptance of people with autism spectrum disorder; and advancing research into causes and better interventions for autism spectrum disorder and related conditions. Through partnerships and collaboration, we are committed to:

- Increasing global understanding & acceptance of people with autism
- Being a catalyst for research breakthroughs
- Increasing early childhood screening & timely interventions
- Improving the transition to adulthood
- Ensuring access to reliable information & services throughout the life span

#### ***Strategic Intent of Autism Speaks Science***

To be a catalyst for research breakthroughs that improve lives today and deliver a spectrum of solutions in the years ahead. This work involves unraveling the biology of autism, including its varied subtypes and dimensions, and translating research findings into life-enhancing solutions.

#### ***Commitment of Autism Speaks Science***

Autism Speaks is committed to collaborating with the autism community to advance research that discovers autism's underlying biology, translates findings into better evidence-based interventions, and tailors and delivers interventions to those who may benefit from them.

#### ***Vision of Autism Speaks Science***

Through our commitment to be a catalyst for research breakthroughs and a collaborator with the autism community, we envision the decade ahead as delivering as fundamental advances in identifying and understanding autism and treating or otherwise supporting people with autism across the diversity of the spectrum.

### **2018 – 2020 Strategic Plan for Science**

Our overarching mission is to be a sustainable engine for the discovery, delivery and implementation of improved options for intervention and support. We will prioritize the following goals and strategies to ensure that funded activities receive sufficient resources to meet their aims, with the acknowledgement that some proposed activities may be delayed until sufficient resources become available.

Importantly, we consider this plan to be a living document that will continue to benefit from review and feedback in the coming years.

This three-year strategic plan for science includes the timeline of January 1, 2018 through December 31, 2020. It will be integrated into the current Autism Speaks Strategic Plan and updated to sync with the next one.

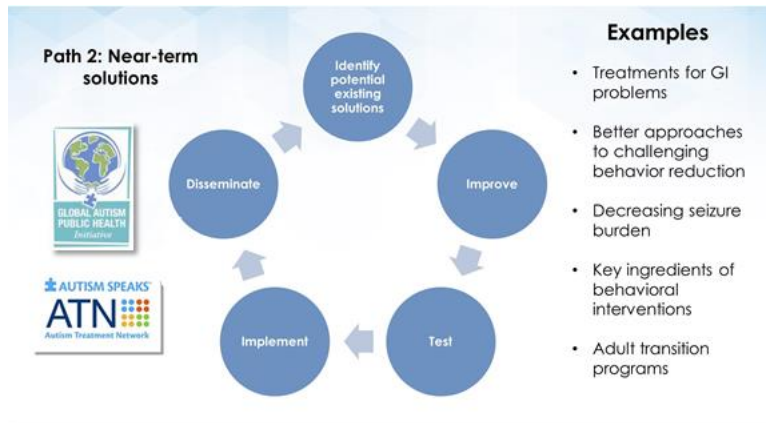
### A Two-Pronged Approach

Autism Speaks is committed to enhancing lives today and accelerating a spectrum of solutions for tomorrow. This vision is reflected in our two-pronged approach to supporting research.

Biological discovery and translational research are rapidly delivering powerful new personalized therapies for many medical and developmental conditions. In autism, this work is currently progressing for the major genetic syndromes associated with the disorder. Autism Speaks is dedicated to furthering this research with the goal of delivering personalized solutions for the broader autism spectrum. (Path 1 illustrated below.) This process is likely to take several years for even the best-characterized autism subgroups and biological processes. Importantly, by “subgroups” we mean not only genetically defined syndromes but also groups sharing nongenetic biomarkers, common symptoms and/or associated medical conditions.



**Meanwhile, individuals and families affected by autism need *solutions now*.** This includes care guidelines and more-effective treatments for autism-associated health conditions such as epilepsy, sleep and GI disorders, as well as associated mental health conditions such as anxiety and depression. We also urgently need evidence-based programs supporting the transition to adulthood and the little-understood issues that arise with aging. (“Path 2” illustrated below)



The Autism Speaks ATN and GAPH programs are ideal platforms for implementing, evaluating and disseminating both the near-term and long-term solutions described above. For all these reasons, Autism Speaks will continue its long-standing approach of “enhancing lives today while accelerating a spectrum of solutions for tomorrow” with our two-pronged strategic plan for science.

**The seven strategic science objectives of this three-year plan – together with the strategies to achieve them – are as follows:**

**1. Support research that uncovers the biology of autism to advance the delivery of personalized therapies and supports**

<i>Activities to implement this strategic objective</i>
<b><i>Using genetics to understand the biology of autism</i></b> <i>Through AGRE and MSSNG, as well as partnerships involving outside genetic-discovery initiatives such as the Simons Simplex Collection, SPARK and the Autism Sequencing Consortium, we will:</i>
A. Complete sequencing of the MSSNG program’s initial 10,000 biological samples, uploading and making them available for global research
B. Require a commitment to open science and the broad availability of data from all researchers using AGRE and MSSNG resources
C. Invite applications for new grants supporting the use of AGRE and MSSNG resources in service of the autism community
D. Facilitate greater access and new partnerships in genomic autism research by indexing global sequencing cohorts and combining sequencing cohorts where feasible
<b><i>Uncovering the role of non-genetic risk factors and gene-environment interactions in autism biology</i></b> <i>By issuing requests for applications and leveraging existing resources, we will:</i>
E. Advance the use of MSSNG data and related resources to investigate gene-environment interactions in autism
F. Partner with outside research groups with databases on environmental and gene-environment risk factors for autism to speed low-cost advances in our understanding of these factors
G. Partner with research groups examining factors that increase or decrease risk of various subgroups of autism as well as social and environmental factors that influence outcomes

## 2. Support research that translates basic discoveries into potential personalized treatments ready for clinical testing

<i>Activities to implement this strategic objective</i>
A. Assist in the development of cohort research registries for interested participants within identified subgroups of autism
B. Partner with the National Center for Advancing Translational Science (NCATS) to conduct an expert/community workshop on selecting promising autism subgroups for translational treatment studies (These subgroups could include those most likely to benefit from treatments that target particular symptoms, associated health conditions, biomarkers, etc.)
C. Issue a funding opportunity for one or more preclinical studies of a personalized medicine or other treatment strategy for an autism subgroup, potentially in partnership with a biotech and patient advocacy organization
D. Issue a funding opportunity for research that distills knowledge of autism subgroups and develops and/or implements clinical practice guidelines for children and/or adults affected by them

## 3. Facilitate the clinical testing of promising life-enhancing interventions, including scalable and sustainable community programs

<i>Activities to implement this strategic objective</i>
A. Develop the Autism Speaks ATN into a Learning Health System Network to support clinical trials, using 2018-2020 baseline funding for developing clinical trials infrastructure
B. Support at least one medium to large clinical trial of a near-term solution for addressing a core autism symptom or a related physical or mental health condition
C. Support the development of evidence-based practices in the transition to adulthood and research that deepens understanding of autism over the lifespan
D. Support the World Health Organization (WHO)/Autism Speaks Parent Skills Training (PST) program and related non-specialist interventions through domestic and international development and testing activities
E. Increase and enhance autism care in primary and specialty care settings by expanding ECHO Autism, the medical tele-training program developed and pilot tested by the ATN.
F. Use the Learning Health System Network model, in partnership with federal agencies, to improve the reach of autism care guidelines, build care capacity and address care disparities at the community level
G. Ascertain outcomes from autism-specific programs supporting the transition from pediatric to adult healthcare

## 4. Improve the measurement of autism and its associated features to enhance screening, diagnosis, subgroup identification and the tracking of change during clinical trials and across the lifespan.

<i>Activities to implement this strategic objective</i>
A. Conduct a research consensus conference on objective measures of autism-related features and outcomes, building on the findings of the 2010 autism measurement conference
B. Issue a targeted grant opportunity to support the testing and clinical use of an objective measure of autism
C. Test promising subjective and objective outcome measures through an ATN clinical trial
D. Support the dissemination and implementation of the Open Source Screening and Diagnostic Tool (OSSDx). When possible, this will be done in global and U.S. locations already pilot testing the WHO/Autism Speaks Parent Skills Training program

**5. Promote consensus building in research and the widespread use of life-enhancing research findings by facilitating engagement among leaders in research, clinical practice and the autism community**

<i>Activities to implement this strategic objective</i>
A. Convene consensus panels on key topics related to controversial issues, personalized medicine, clinical care and other services important to patients and families
B. Provide practical and easily accessible web-based vehicles for sharing scientific findings and practice guidelines with healthcare providers, educators and families
C. Complete and share the ATN Clinical Care Manual and its associated clinical algorithms
D. Translate ATN/AIR-P tool kits into additional, widely used languages
E. Increase dissemination partnerships, including but not limited to the International Society for Autism Research; The Autism Speaks Advocacy Leadership Network; community-based networks (e.g. African-American, Latino-American, Chinese American, adult self-advocates, rural communities); Autism Speaks ATN and Field offices; National Academy of Medicine, American College of Medical Genetics; The American Public Health Association and the American Psychological Association; NIH/CDC and other domestic and international private and public funding agencies
F. Increase action and implementation activities among the members of GAPH's advocacy networks
G. Support the creation of new methods for sharing best practices such as the expansion of ECHO Autism, the WHO/Autism Speaks Parent Skills Training program and other e-learning technologies and culturally adapted programming

**6. Continually review research areas and Autism Speaks science activities to identify those ripe for culmination or transition to other funding sources and to ensure that new funding areas complement rather than duplicate those supported by other funders**

To optimize the return on its research investments, we will continually evaluate research areas and priorities for their potential to draw outside funding or otherwise transition from Autism Speaks support.

<i>Activities to implement this strategic objective</i>
A. Quarterly review of research portfolios by assigned science staff members, with semi-annual reporting to the Medical and Science Advisory Committee.
B. Annually report on research concluded or transitioned to other funding sources

**7. Broadly and effectively communicate our science strategic plan and ongoing progress against its goals, with emphasis on engagement with the autism community**

<i>Activities to implement this strategic objective</i>
A. Communicate this plan in lay friendly yet detailed and meaningful forms through multiple vehicles and media
B. Create and support collaborative and outside programming and venues for lay-friendly explanations of scientific concepts crucial to autism research. For example, webcasts and podcasts that describe new concepts or findings in epigenetic or gene-environment interaction studies
C. Deliver regular reports to the Autism Speaks leadership on recent science accomplishments, including funded publications and innovations

**Timeline and Deliverables**

We acknowledge that some of these metric activities may be delayed until sufficient resources become available.

**1. Support research that uncovers the biology of autism subgroups (as defined by genetics, biomarkers, symptoms and/or associated health conditions) to advance the delivery of personalized therapies and supports**

<i>Three-year activities to implement this strategic objective</i>
* Starting in January 2018, include provisions for open science and increased data availability in all research grant contracts
* By the end of 2018, merge at least one additional sequencing cohort with MSSNG for availability to researchers
* By 2019, support multiple small grant applications for using AGRE and MSSNG resources
* By 2019, make at least 10,000 whole genome sequences and associated phenotypic data available to researchers through MSSNG
* By 2020, identify at least one opportunity to partner with and enhance an existing environmental risk project such as the Environmental Epidemiology of Autism Research Network
* By 2020, increase the availability of environmental risk data within MSSNG and/or support the acquisition of sequencing data for a large cohort with environmental risk data

\* By 2020, support a research consensus conference focused on environmental risk factors and the advancement of research on gene-environment interactions

\* By 2019, establish a partnership with at least one autism-associated genetic syndrome advocacy or research group and/or a broader program

## 2. Support research that translates basic discoveries into potential personalized treatments ready for clinical testing

*Three-year activities to implement this strategic objective*

\* By 2019, collaborate with other autism research funders to support a conference on identifying autism subgroups (defined by shared symptoms, associated medical conditions, genetics or other biomarkers) and the most promising methods for developing targeted treatments

\* By 2019, fund one or more projects focused on early translational activities for a newly identified autism subgroup, including the collection of physical and mental health history, development of care guidelines, bioinformatic analysis of genes and associated pathways, bioinformatic analysis of potential therapeutic targets and/or development of translational blueprints

\* By 2019, fund and/or secure a funding partner for a pre-clinical study of a potential therapeutic for an autism subgroup and/or secure additional industry contracts to test potential therapeutics in the PACT program by 2020

\* By 2020, work with at least one group focused on an autism-associated genetic syndrome to establish and/or enhance a registry that includes common data fields to facilitate coordinated work between other autism-associated genetic syndrome registries

## 3. Facilitate the clinical testing of promising life-enhancing interventions, including scalable and sustainable community programs

*Three-year activities to implement this strategic objective*

\* By 2019, transition the existing ATN registry database into a broader registry that collects some information on the majority of individuals seen in clinics, while continuing deeper information collection on a subset of patients

\* By 2019, complete at least one randomized controlled trial (RCT) and six feasibility trials for the WHO/Autism Speaks Parent Skills Training (PST) program, including one in the United States

\* By 2019, support WHO in the finalization and global release of an official PST manual

\* By 2020, publish at least one RCT report and two reports on program feasibility or implementation of the PST program.

\* By 2020, transition clinical data collection at ATN sites to include electronic data collection and/or medical records capture that rapidly uploads to an easily accessed database

\* By 2020, complete at least one ATN pilot study or small clinical trial and one medium to large clinical trial evaluating an alternative treatment approach that is currently used by autism families despite inadequate evidence of safety and effectiveness

\* By 2020, initiate funding or co-funding of at least one phase I or II clinical trial of a potential therapeutic for an autism-associated genetic subtype or a biologically stratified autism subgroup (e.g. idiopathic autism with elevated inflammatory markers)

* By 2019, fund at least two investigations specifically focused on testing the efficacy or comparative effectiveness of interventions for improving the transition to adulthood or for increasing our understanding of the long-term physical, mental health or daily living challenges of adults with autism.
* By 2020, ATN sites will provide ECHO Autism to an additional 150 primary care and community care professionals and groups.
* By 2020, the ATN will adapt ECHO Autism to use tele-health technology and the ATN Care Manual to provide technical assistance to 20 autism specialty centers outside of the current ATN network, in North America and/or globally.
* By 2019, the ATN will develop five video versions of its tool kits and test the feasibility of conducting remote Facebook Live chats with providers to discuss tool kits and address frequent questions .
* By 2020, the ATN’s Learning Health System Network will add five sites.
* By 2020, the ATN will develop and disseminate five additional clinical algorithms to guide medical best practices in autism.
* By 2020, the ATN will conduct a study to evaluate the use and effectiveness of the ATN/AIR-P tool kits and guidelines.

**4. Improve the measurement of autism and its associated features to enhance screening, diagnosis, subgroup identification and the tracking of change during clinical trials and across the lifespan**

<i>Three-year activities to implement this strategic objective</i>
* By 2019, complete a consensus conference focused on identifying objective and clinical measures of autism-related features and outcomes ripe for dissemination and implementation
* By 2019, complete one multi-site validation trial of the draft Open Source Screening and Diagnostic Tool (OSSDx)
* By 2019, partner with at least one public or private funding agency to enhance dissemination and impact of the measures described above
* By 2020, publish at least one report or commentary on the meeting outcome in a peer-review journal
* By 2020, fund a research project that supports real-world clinical validation and implementation activities for an objective measure of autism or related features. This project may be conducted by either an independent investigator or an early career investigator under the mentorship of a senior investigator.
* By 2020, the ATN will embed the testing of a subjective and/or objective autism outcome measures within at least one pilot and one large clinical trial.
* By 2020, establish formal governance for OSSDx at the annual meeting of the International Society for Autism Research (INSAR) and issue co-funding call with INSAR for using this instrument in diverse settings

**5. Promote consensus building in research and the widespread use of life-enhancing research findings by facilitating engagement among leaders in research, clinical practice and the autism community**

<i>Three-year activities to implement this strategic objective</i>
--



* By 2019, co-fund at least two regional international research meetings focusing on clinical and applied science and/or public health
* By 2019, co-fund at least one mentorship program to enhance the spectrum and diversity of voices in the autism self-advocacy community
* By 2019, co-fund at least four regional network meetings or programs focusing on community-level data collection and dissemination of the Parent Skills Training (PST) program or open-source diagnostic tool (OSSDx). These will include at least two activities in the United States (e.g. involving African American, Asian American or other underserved communities)
* By 2020, create and make available a web-based vehicle for sharing scientific findings and practice guidelines with healthcare providers, educators and families
* By 2020 translate an additional ten ATN/AIR-P tool kits for non-English speaking audiences
* By 2020, fund at least one National Academy workshop on an Autism Speaks scientific priority
* By 2020, host two Autism Leadership Network conferences with emphasis on dissemination of PST and OSSDx experiences and community-based data collection for evaluation
* By 2020, fund or co-fund at least two community-based data collection projects on PST and/or OSSDx, one in the U.S. and one abroad
* By 2020, begin initial pilot the electronic version of PST
* By 2020, begin initial pilot of the e-version of OSSDx

**6. Continually review research areas and Autism Speaks science activities to identify those ripe for culmination or transition to other funding sources and to ensure that new funding areas complement rather than duplicate those supported by other funders.**

<i>Three-year activities to implement this strategic objective</i>
* Each year, complete at least two semi-annual reviews for all active research projects
* Each year, provide at least one comprehensive report on each project or activity to the Medical and Science Advisory Committee
* By the end of 2018, provide an annual report to the Autism Speaks Board and the Medical and Science Advisory Committee on research culminated or transitioned to other funding sources

**7. Broadly and effectively communicate our science strategic plan and ongoing progress against its goals, with emphasis on engagement with the autism community**

<i>Three-year activities to implement this strategic objective</i>
* By January 2018, complete widespread distribution through each of the sources listed above, while continuing to look for methods to maximize reach
* By April 2018, submit a report of the strategic planning survey to an autism research journal
* Each year, co-host and/or provide other support for at least four webcasts, webchats and/or podcasts on prioritized avenues of research, in partnership with other autism advocacy and science organizations and/or public agencies
* Each year, deliver monthly science accomplishment reports to the Autism Speaks Board and Medical and Science Advisory Committee

\* By 2019, begin conducting media training for autism researchers, including Autism Speaks research fellows and other funded investigators, to enhance public interest and media coverage of their work and ensure that research findings are conveyed with appropriate context and perspective

### **Supporting Objectives:**

In addition, this strategic plan hinges on additional commitments to action in three supporting activity areas. They are:

- 1. Engagement of people with autism and their families.** We will sustain and increase our efforts to engage the autism community in shaping and driving the programs and other activities we undertake in pursuit of this strategic plan for science, including inclusion in the science review process.
- 2. Support and development of the next generation of autism researchers.** We will re-invigorate the review process for our fellowship programs with increased inclusion of people with autism, parents and other stakeholders, accompanied by enhanced scientific-review training and guidelines for our non-scientist reviewers.
- 3. Grants management.** We will improve our peer-review of research grants with special focus on enhancing the reliability of peer reviewers for each application, while including more self-advocates and family members in the process, increasing the efficiency of progress reporting and payment and improving our process for tracking funding outcomes.

### **Current Autism Speaks Science Initiatives**

Current Autism Speaks science programs span the field of autism research from basic discovery to the testing and dissemination of improved medical guidelines, behavioral therapies, supportive technologies and other evidence-based solutions.

Our AGRE and MSSNG genomics program will continue to play key roles in facilitating the biological discoveries that can be translated into personalized care and therapeutics. Our PACT program supports the preclinical testing needed to advance basic discoveries through the pharmaceutical pipeline to human trials.

The Autism Speaks Autism Treatment Network (ATN) and Global Autism Public Health (GAPH) program are crucial for evaluating methods already in use and developing and implementing care improvements across North America and globally. This work emphasizes solutions to close the care gap experienced by low-resource communities at home and abroad. The ATN has the additional potential to be a vehicle for moving potential personalized therapies from pre-clinical studies to trials enrolling children and adults with autism. Below is a brief history and description of these programs and their successes.

#### **Autism Genetic Resource Exchange (AGRE)**

AGRE is the largest private, open-access repository of clinical and genetic information dedicated to supporting autism research, with more than 2,000 families in its database. Since its inception in 1997, AGRE has been cited in more than 165 scientific papers and has led to breakthroughs in understanding autism's causes and risk factors with



discoveries that are leading to more effective treatments. Currently, more than 150 research groups worldwide are using AGRE resources. Many AGRE families are now contributing their banked biological samples and clinical information to MSSNG, Autism Speaks signature whole genome database and research program.

### **MSSNG**

MSSNG (pronounced “missing”) is a groundbreaking collaboration between Autism Speaks, Verily and Toronto’s Hospital for Sick Children to create the world’s largest genomic database on autism. By sequencing the DNA of over 10,000 people from families affected by autism, MSSNG will help researchers answer the many questions we still have about the disorder.



Thanks to the Google Cloud, we are making this vast amount of genomic information accessible at no charge to qualified researchers everywhere, along with a cutting-edge tool kit of analytic programs. Already, the completed sequencing of the first 5,000 whole genomes has led to groundbreaking discoveries about subtypes of autism and their associated medical conditions. We anticipate that, as the MSSNG project grows, researchers will identify many biological subtypes and dimensions of autism, leading to more personalized and effective treatments.

### **Preclinical Autism Consortium for Therapeutics (PACT)**

In 2013, Autism Speaks established PACT to address the bottleneck preventing promising autism medicines from moving out of the laboratory and into the human trials needed to demonstrate safety and efficacy. This blockage was the lack of high-quality animal models for early drug testing.



With its first grants, PACT engaged the field’s leading experts to develop six precedent-setting animal models of known genetic subtypes of autism. Thanks to extensive behavioral and genetic characterization, our funded researchers have established that each of these mouse models is a reliable testing platform for compounds that can address the core autism symptoms associated with one of six known autism-linked gene variants (Shank3, Grin2, Pten, Fmr1, Cntnap2 and Gabrb3).

To date, four pharmaceutical companies have approached PACT with interest in using these animal models to screen their libraries of proprietary compounds for their potential to ease disabling autism symptoms. This has emboldened us to set a goal of facilitating the screening of at least one promising medicine each year.

### **Autism Treatment Network (ATN)**

Our ATN is a collaboration of Autism Speaks and many of the finest children’s hospitals and academic medical institutions in North America, focusing on the multi-disciplinary medical care of children and teens with autism. Together, these centers develop evidence-based protocols and standards of care for the challenging medical conditions associated with autism. ATN clinicians share the best practices they’ve developed with physicians and medical facilities across North America, with the aim of improving the outcomes for all people with autism.



The ATN acts as a platform for research and maintains a voluntary patient registry that includes ongoing collection of medical and behavioral information from more than 7,000 children with autism.

Integral to this work is the ATN’s role as the U.S. Health Resources and Services Administration’s Autism Intervention Research Network on Physical Health (AIR-P). The AIR-P focuses on research to improve the

physical health of children with autism. This research builds on the ATN's clinical work to further improve the lives of patients and their families. As a joint network, the ATN/AIR-P has published more than 100 scientific papers, five medical guidelines for addressing associated health conditions and 23 tool kits on autism-related medical issues.

### **Global Autism Public Health Initiative (GAPH)**

Autism Speaks is committed to helping meet the needs of children and adults affected by autism in underserved communities at home and abroad. Through GAPH, we collaborate with families, professionals, advocacy groups and governments in more than 70 countries, with the shared goals of better understanding the global issues surrounding autism and enabling the practical and effective delivery of care.



Working with United Nations agencies including the World Health Organization (WHO), we help nations create feasible, effective and sustainable public health programs and research networks that address the needs of children, adults and families affected by autism.

As facilitators, technical advisors and co-funders, we strive to:

- Engage local families and communities
- Amplify our partners' investments in autism health programs
- Support innovation that improves delivery of sustainable services
- Launch vital research that is more practical and affordable to perform abroad.

In the United States, GAPH enhances public health research and helps shape public health policies to promote children's behavioral health and meet the needs of our growing autism community.

Our collaborators in the U.S. include:

- The Centers for Disease Control and Prevention - The National Institutes of Health
- The National Academies of Science, Engineering and Medicine
- The Data Resource Center for Child and Adolescent Health
- Minority, immigrant, rural and other underserved communities.