Jaguar Gene Therapy
Two Conway Park
150 N. Field Drive, Suite 300
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www.jaguargenetherapy.com

July 8, 2026

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Developmental Milestone Study Questions

Q: What is the developmental milestone study?
A: Caregivers of individuals with Phelan-McDermid syndrome (PMS) are invited to participate in an online research study of developmental milestones. Participation is remote, completed through an online application, and compensation may be provided for completing study-related surveys. There is a total of three surveys in the study – one taken at enrollment, one taken six months later and the final one taken 12 months later.

This research study aims to better understand how developmental milestones, or skills, develop or may be lost over time in individuals living with Phelan-McDermid syndrome. Understanding how skills are gained, lost or regained helps researchers better understand PMS and can provide a potential reference, or comparison, for treatment related benefits in a clinical trial. Jaguar is exploring how the data from this study may help accelerate the development process for treatments like JAG201 and other investigational treatments for PMS. This has been a successful strategy in the Rett syndrome space. You can learn more by viewing recent investor presentations that describe the progress of a milestone-focused regulatory pathway from two companies: Neurogene and Taysha Gene Therapies.

Q: Why is participating in the developmental milestone study important?
A: In addition to providing data that may directly inform how treatments are evaluated, caregiver insights generated in the survey provide valuable real-world information that helps researchers understand which developmental milestones are most meaningful to families. This knowledge helps guide future treatment research and support development programs. As a caregiver of an individual with Phelan-McDermid syndrome, your insight is essential to understand the natural history of PMS and what meaningful treatment benefit looks like for you and your family.

Q: How could participating in the developmental milestone study help future research?
A: Information collected in this study may help researchers better understand how developmental skills are attained or lost over time in individuals with Phelan-McDermid syndrome. This study collects what is considered natural history data, however this study is not part of the Developmental Synaptopathies Consortium's (DSC) natural history study.* Natural history data like this could support the design of future clinical trials by helping researchers understand how developmental milestones may be gained because of being treated with an investigational treatment.

Specifically, these natural history data provide a reference for understanding what skills or milestones may be gained through the natural trajectory of PMS and what may be considered a treatment-specific effect. These natural history data may help researchers explore alternative study designs that may be beneficial for evaluating treatments in rare disease. Participation in this study does not guarantee that any specific study design changes will occur.

*If you currently participate or plan to participate in the DSC natural history study, you are still eligible to participate in Jaguar's developmental milestone study.

Q: Who is eligible to participate in the developmental milestone study?
A: You may qualify for the study if:

- You currently reside in the United States and are a caregiver (parent or guardian) of someone diagnosed with PMS
- You are an adult based on the age of majority in your state or territory of residence
- Your loved one is between ages 2 and 30 years

- You are willing and able to complete online surveys in English

Final eligibility will be determined by the study team based on study requirements.

Please note: inclusion/exclusion criteria for the study have been updated since the community webinar held in April and we encourage you to visit www.pmscaregiverstudy.com for more details.

Q: The study asks for participants to provide supporting documentation for an individual's developmental milestone achievement, loss or regain. What types of supporting documentation are appropriate and acceptable? Is there any type of documentation that is not acceptable?
A: Supporting documentation can include a wide range of materials that reflect the same time frame as the developmental skill gain, loss, or regain reported. Examples include photos, audio or video recordings, medical records, school or therapy records, personal records, baby books, calendars, journal entries, or similar documentation. Note that documentation does not need to be formal medical assessments or therapy records to be considered for the study.

We ask that participants do not submit photos or videos that show someone using the bathroom or other such activities as we seek to preserve the privacy and dignity of individuals with PMS.

Q: Can I still participate in the developmental milestone study if I have little to no supporting documentation?
A: Yes, caregivers can absolutely take part in the study even if they have little to no supporting documentation. We ask participants to share any documentation they may have and feel comfortable providing, but lack of documentation does NOT exclude someone from participating.

Some cues that could be helpful to think about in terms of potential documentation or timeframe of milestone gain, loss or regain could include a major life event like a move, a new school, birth of new child, a trip or a holiday.

Q: Do I need to travel to participate in the study?
A: No. All study activities are completed online from your computer or handheld device.

Q: How long does participation in the study last?
A: The first survey is the longest and may take several hours to complete – we estimate 4 to 8 hours. The survey can be completed over multiple sessions over a three-week period to help ensure you can complete it at times that are convenient for you. If completing the survey within the three-week time period is a concern, we are happy to discuss your specific situation. The follow-up surveys (taken 6 months and 12 months after the first survey) will take less time to complete – we estimate 1 to 2 hours.

Q: How long does it take to complete the surveys in the developmental milestone study?
A: The first survey may take several hours and can be completed over multiple sessions over a three-week period. Follow-up surveys take less time.

Q: Will the information I provide in the study be kept confidential?
A: Yes. All study data is stored securely and used only for research purposes.

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Q: Is compensation available for those who participate in the developmental milestone survey?
A: Yes. Participants will be compensated for the completion of the initial survey, for completion of the 6-month follow-up survey, and for completion of the 12-month follow-up survey. Payments will be made at the completion of each survey. Participation and compensation details will be outlined in the Informed Consent Form, and the study team will answer any questions you may have.

Q: Will participating in the developmental milestone survey provide access to a clinical trial or gene therapy?
A: No. Participating in this study does not provide access to clinical trials or gene therapy, and it does not affect eligibility for future trials. This research is designed to gather important information from caregivers to support future research efforts.

General Gene Therapy Questions

Q: What is gene therapy?
A: Gene therapy involves delivery of healthy copies of genes into the body with the aim of restoring the function of target cells. Jaguar's gene therapy programs use an adeno-associated viral (AAV) vector-based delivery, meaning AAV functions as a type of vehicle (or vector) to deliver functioning genes into the target cells. AAV has been shown to be an effective vector because it is nonpathogenic (meaning it is not capable of causing illness) but very effective at gaining access to the target cells. To be used as a vector for gene delivery, the viral DNA of AAV is removed and replaced with a gene that is intended to have a therapeutic benefit for a patient suffering from a genetic disease. After the AAV vector delivers its genetic payload to the nucleus of a cell, the gene is then transcribed and translated to produce a functional protein. The gene will persist in the nucleus as an episome, separately from the chromosomes. The patient's body then breaks down and processes the AAV vector.

You can view a brief animated video created by Jaguar for younger audiences that explains gene therapy here.

Q: Does gene therapy alter a person's DNA?
A: This depends on the type of gene therapy utilized. We have specifically selected AAV as a vector in part due to its low likelihood for altering the patient's DNA. While AAV vectors primarily deliver a gene to the nucleus which then exists separately from the patient DNA, there have been some cases where AAV-delivered gene inserts into (combines with) patient DNA in human clinical trials. To date, there is no evidence that AAV-delivered gene therapy has led to development of cancer.

Q: Are there potential risks associated with AAV vectors?
A: Vector-associated safety risks have been reported in both animals and human clinical studies of investigational AAV gene therapies, as well as in post-marketing experience with approved gene therapies. Sometimes the immune system overreacts to the vector, leading to complications affecting the liver, the brain or your body's ability to form clots. To decrease the likelihood of immune system-linked risks, clinical trials may screen for antibodies to AAV vectors and require medicines to decrease the patient's immune response. This is one of the reasons the clinical trial includes outcomes measures to evaluate and understand the immune response to treatment.

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JAG201 Mechanism of Action, Administration and Therapeutic Goals Questions

Q: How does JAG201 work?

A: *SHANK3* haploinsufficiency leads to dysfunction at the synapses, or interaction points between neurons, disrupting communication between nerve cells. It causes a reduction of several key neuron receptors and signaling proteins, resulting in impaired synapse formation between neurons. Adequate synapse function is essential for neuron-to-neuron communication, which is the basis for learning and cognitive function. JAG201 delivers a functional *SHANK3* minigene* via an adeno-associated virus serotype 9 (AAV9) vector to target neurons in the central nervous system. The therapy is designed to deliver proper SHANK3 protein levels and to durably restore the synaptic function required for learning and memory, which underlie appropriate neurodevelopment and maintenance of communicative, motor, cognitive and social skills.

*A minigene is a shortened form of the gene that retains the key functional components of the genetic sequence. The *SHANK3* minigene was created by removal of unessential parts of the *SHANK3* gene in order to allow the DNA to fit within the AAV vector.

Q: How is JAG201 administered?

A: JAG201 is administered via intracerebroventricular (ICV) injection. The procedure is performed by a neurosurgeon in the operating room under anesthesia and takes approximately 30 minutes. This is followed by observation and discharge within approximately 48 hours.

ICV administration is an injection directly into the brain using a catheter, or tubing, into a space known as the lateral ventricle which contains cerebrospinal fluid (CSF). Humans have two ventricles in the brain, one in each hemisphere, and JAG201 will be injected into one ventricle. A neurosurgeon, who is experienced at performing this type of surgery, will perform the procedure and will know how to guide the catheter into the right space by looking at pictures taken of the patient's brain using imaging such as MRI or CT before the procedure. This method was selected with the goal of delivering JAG201 directly to the target cells in the brain and central nervous system and is supported by the preclinical studies conducted with JAG201 to evaluate its potential benefit and safety profile in animals. You can view Jaguar's published preclinical data on the biodistribution and tolerability of JAG201 in non-human primates following ICV injection here.

Outside of gene therapy, ICV administration is utilized for short-term and long-term delivery of certain approved medicines into the brain and central nervous system (CNS). According to published research, more than 20,000 procedures are done annually in the U.S.[1]

Q: How do you get the AAV to go to the desired location (i.e., to the cells lacking in SHANK3)? Does it go to the entire brain?

A: JAG201 is administered via intracerebroventricular (ICV) injection. The procedure is performed by a neurosurgeon in the operating room under anesthesia and takes approximately 30 minutes. This is followed by observation and discharge within approximately 48 hours.

[1] Sekula RF, Cohen DB, Patek PM, Jannetta PJ, Oh MY. Epidemiology of ventriculostomy in the United States from 1997 to 2001. Br J Neurosurg. 2008 Apr;22(2):213-8. doi: 10.1080/02688690701832084. PMID: 18348016.

ICV administration is an injection directly into the brain using a catheter, or tubing, into a space known as the lateral ventricle which contains cerebrospinal fluid (CSF). Humans have two ventricles in the brain in each hemisphere of the brain, and JAG201 will be injected into one ventricle with the goal of delivering JAG201 broadly to the regions of the brain and central nervous system that may be relevant to Phelan-McDermid syndrome (PMS). This method was selected with the goal of delivering JAG201 directly to the target cells in the brain and central nervous system and is supported by the preclinical studies conducted with JAG201 to evaluate its potential benefit and safety profile in animals. Additionally, JAG201 expression is controlled by a neuron-specific promoter to ensure the *SHANK3* minigene is only expressed in neuronal cells.

Outside of gene therapy, ICV administration is utilized for short-term and long-term delivery of certain approved medicines into the brain and central nervous system (CNS). According to published research, more than 20,000 procedures are done annually in the U.S.[1]

Q: Has intracerebroventricular (ICV) administration of AAV been done in humans before? What is known about how those patients fare in the long term?
A: Yes. There are multiple investigational AAV-based gene therapy treatments currently in clinical trials that are administered via a one-time ICV injection. These studies are ongoing and long-term data and outcomes in these participants are pending.

Outside of gene therapy, ICV administration is utilized for short-term and long-term delivery of certain approved medicines into the brain and central nervous system (CNS). According to published research, more than 20,000 procedures are done annually in the U.S.[1]

To learn more about gene therapy routes of administration, including ICV, please view ASGCT's Lunch & Learn on the topic.

Q: Will immune system suppression be required for the administration of JAG201?
A: Short-term immune suppression will be required and is standard for AAV-based investigational gene therapy treatments to prevent immune reaction to delivery of the gene therapy.

Q: What exactly is JAG201 designed to correct or improve in an individual with PMS?
A: JAG201 is intended to address the root cause of the disease and potentially improve cognitive, functional and behavioral abnormalities observed in PMS. The therapy is designed to deliver the SHANK3 minigene and support functional SHANK3 protein levels, with the goal of durably supporting synaptic function, which is essential for learning and memory, and which underlie appropriate neurodevelopment and maintenance of communicative, motor, cognitive and social skills. Results from the initial clinical study will help inform further study development.

Q: How can you control for over-expression of *SHANK3*?
A: The *SHANK3* minigene is under the regulation of the human synapsin 1 promoter, which limits expression to neuronal cells.

Q: Does JAG201 have the potential to be a cure for PMS?
A: JAG201 is being studied as a potential treatment for PMS by addressing the underlying genetic cause of the disease. The goal is to evaluate whether JAG201 may have a lasting impact on the disease including the associated behavioral,

developmental, and cognitive abnormalities observed in individuals with disorders resulting from *SHANK3* mutations or deletions. It is not known whether JAG201 will be safe or effective in people with PMS, and it should not be considered a cure at this time. Results from the initial clinical study will help inform further development of JAG201.

Q: Will the effect of JAG201 be durable over time? Do brain cells/neurons die?
A: Given the low potential for cellular division in the brain, a one-time JAG201 ICV gene delivery may have the possibility for lasting durability in neurons. Neurons are generally non-dividing, compared to another target tissue such as the liver, which has a higher rate of cell turnover. However, the durability of JAG201's effect in individuals with PMS is not yet known.

JAG201 Preclinical Data Questions

Q: What preclinical studies have been done to date with JAG201?
A: Preclinical (animal models) studies are an important and required step in evaluating new potential treatments before human clinical trials. Preclinical data for JAG201 in rodent and non-human primate models of *SHANK3* insufficiency have been encouraging and support further clinical evaluation.

Q: Has Jaguar presented any preclinical data for JAG201?
A: Yes. In May 2024 at the Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT), Jaguar presented the first preclinical efficacy data for JAG201 following a single intracerebroventricular (ICV) injection in mice. The proof-of-concept (POC) data show that in a mouse model of *SHANK3* deficiency, which mimics many of the features of humans with loss of one functional *SHANK3* gene, JAG201 treatment resulted in statistically significant improvements in neurobehavioral outcomes involving measures of restorative sleep, motor and explorative behavioral deficits, and motor-coordination deficits vs. untreated control animals lacking both copies of *SHANK3*. Additionally, JAG201 treatment resulted in broad and persistent delivery of *SHANK3* throughout the brains of treated animals, suggesting that these neurobehavioral improvements can be sustained over time following a single ICV treatment with JAG201. You can view the data here on Jaguar's website under the "Disorders with *SHANK3* mutation or deletion" section.

Q: Can you share the results you saw in non-human primate and mouse studies?
A: To date, we have presented two sets of preclinical data. You can see the published information here on our website under the "Disorders with *SHANK3* mutation or deletion" section. These data were used to support our investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA). We are continuing to work to publish additional data from our preclinical studies.

JAG201 First-in-human Clinical Trial Eligibility and Enrollment Questions

Q: What is a Phase 1 clinical trial?
A: In a Phase I clinical trial, a treatment is tested in a small group of people for the first time. The purpose is to study the treatment to learn about safety, tolerability and dose. To learn more about clinical trials, you can visit https://www.fda.gov/patients/drug-development-process/step-3-clinical-research.

Q: Do you anticipate the lower dose in the initial clinical trial to be effective?
A: We have selected an initial dose for the first-in-human (FIH) clinical trial based on preclinical studies in animals and

the overall safety considerations for the study. We are also evaluating an additional escalated dose to help assess safety, tolerability, and whether JAG201 shows signs of activity at different dose levels.

Q: Why will dosing be done one at a time?
A: JAG201 will be evaluated in humans for the first time in this initial clinical study. Although the starting dose is supported by preclinical studies in animals, we plan to dose one patient at a time to allow for thorough safety evaluations of individual patients. If the gene therapy is determined to be well tolerated in the first patient, then dosing of the next patient can proceed. This approach is not unusual in early-stage gene therapy clinical trials, particularly for the first few patients that receive a particular dose. It allows a Sponsor (in this case, Jaguar) and the United States Food and Drug Administration (FDA) to review safety information and make necessary adjustments to the clinical trial and dosing of subsequent patients if a safety concern arises.

Q: Will every pediatric trial participant receive the same exact dose? Is it age or weight dependent?
A: We have selected two doses for two cohorts to use in the initial clinical trial based on preclinical studies in animals and overall safety considerations for the study. Families will be informed of the exact dosage a participant may receive during the screening process.

Q: Is it possible for a trial participant to be re-dosed?
A: JAG201 is being investigated as a single ICV-administration treatment.

Q: How do I enroll my child in the initial clinical trial?
A: Study enrollment is now open at three trial sites: Seaver Autism Center at Mount Sinai, Rush University and Boston Children's Hospital.

Enrollment activities are managed through the trial sites, which can be contacted using the following information.

- United States, New York
  Seaver Autism Center at Mount Sinai
  New York, New York, United States, 10029
  Contact: Serena Cai
  Phone: 212-241-6231
  Email: serena.cai@mssm.edu
  Principal Investigator: Alex Kolevzon, MD

- United States, Illinois
  Rush University
  Chicago, Illinois, United States, 60612
  Contact: Giulia DiMarco
  Phone: 312.942.9841
  Email: giulia_dimarco@rush.edu mailto:
  Principal Investigator: Elizabeth B Kravis, MD, PhD

- United States, Massachusetts
  Boston Children's Hospital
  Boston, Massachusetts, United States, 02115
  Contact: Anna Cronin
  Phone: 617-919-3499
  Email: anna.cronin@childrens.harvard.edu
  Principal Investigator: Siddharth Srivastava, MD

Please visit our clinical trial listing at clinicaltrials.gov for the most current information related to clinical trial sites.

We encourage families with children with PMS aged 12 to 36 months who have interest in the JAG201 clinical trial to explore enrolling in a Phelan-McDermid syndrome natural history study. The Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai in New York City, Rush University in Chicago and Boston Children's Hospital in Boston are actively enrolling patients aged 12 to 36 months.

For information on participating in a natural history study, please reach out directly to the following contacts:

- Seaver Autism Center at Mount Sinai
  New York, New York, United States, 10029
  Contact: Joyce Haddad
  Email: joyce.haddad@mssm.edu
  Currently enrolling ages 12-36 months

- Rush University
  Chicago, Illinois, United States, 60612
  Contact: Lizzy Fitts
  Email: Elizabeth_L_Fitts@rush.edu
  Currently enrolling ages 12-36 months

- Boston Children's Hospital
  Boston, Massachusetts, United States, 02115
  Contact: Anna Cronin
  Email: anna.cronin@childrens.harvard.edu
  Currently enrolling ages 12-36 months

Note that travel stipends may be available for participants in PMS natural history studies at Mount Sinai, Rush University and Boston Children's Hospital, including the Developmental Synaptopathies Consortium (DSC) natural history study. Please inquire with the Phelan-McDermid Syndrome Foundation.

Q: Why do you encourage participation in PMS natural history studies? What is the value?
A: Natural history studies have historically been used by clinical researchers to understand disease progression. More recently, these studies have been utilized to support clinical development in rare diseases. For example, natural history data have served as external comparators to support rare disease treatment approvals when it is unethical or unfeasible

to evaluate the treatment with a randomized controlled trial design.

The more individuals with PMS who participate in natural history studies, the stronger the natural history data for the disease may become. A strong, robust set of natural history data can help researchers, sponsors, and regulators better understand PMS and may support the development and evaluation of potential treatments for PMS. In other words, participating in PMS natural history studies can help improve the information available to support future PMS treatment development and regulatory review.

As Jaguar expands its clinical program, we will first consider individuals that have participated in one of the ongoing PMS natural history studies, including the DSC natural history study, as their natural history dataset will provide an important pre-treatment comparator. Note that participation in the developmental milestone study does not provide preferential access to clinical trials or gene therapy, and it does not affect eligibility for future trials.

Q: What is the screening process for trial enrollment?
A: Following the patient's legally authorized representative (LAR) providing informed consent, patients will undergo screening to determine eligibility for the study. Screening will begin with determination of key eligibility criteria, including genetic status and medical history in addition to a number of baseline assessments. Patients will be evaluated by the study team to determine whether they meet all eligibility criteria and can receive JAG201.

Q: How many participants will you enroll in this first trial? Why?
A: The first clinical trial for JAG201 is designed to evaluate the safety, tolerability and dose of the JAG201 treatment. As a safety study and dosing trial designed to inform the future development of JAG201, we are enrolling a small number of participants (target of 6-10). Depending on the outcomes and learnings from this first trial, we aim to expand the trial to enroll additional patients as early as 2027.

As this is a first-in-human clinical trial, we will monitor safety outcomes in each trial participant closely and anticipate that there may be communications with the FDA after dosing participants. These ongoing discussions with the FDA could inform or determine potential changes to study design including enrollment criteria as the trial progresses.

Q: With such a small number of participants in the trial, how will eligible participants be prioritized?
A: Generally speaking, the first cohort of participants will be prioritized by age with the youngest eligible participants given preference. We are prioritizing age because we believe treating individuals that are still actively undergoing development may provide greater potential for evaluating the benefit of JAG201. Additionally, preference will be given to individuals who have participated in the Developmental Synaptopathies Consortium (DSC) PMS natural history study or are eligible to participate in an ongoing natural history study. Mount Sinai, Rush University and Boston Children's Hospital are currently accepting participants for natural history in the age range of 12-36 months.

Note that participation in the developmental milestone study does not provide preferential access to clinical trials or gene therapy, and it does not affect eligibility for future trials.

Q: Will prioritization change, especially in terms of age, as the first-in-human trial progresses? What about in the second cohort?
A: As we continue to enroll participants in the second cohort, we are considering all ages (2-9 years), but decisions will be made based on overall criteria to determine the optimal candidates for participation. We will continue to give

preference to individuals who have participated in the Developmental Synaptopathies Consortium (DSC) PMS natural history study or are eligible to participate in an ongoing natural history study. Mount Sinai, Rush University and Boston Children's Hospital are currently accepting participants for natural history in the age range of 12-36 months.

Note that participation in the developmental milestone study does not provide preferential access to clinical trials or gene therapy, and it does not affect eligibility for future trials.

Q: Will Jaguar be reaching out directly to specific families about participating in the initial clinical trial?
A: No. Enrollment for the initial clinical trial will be managed through the trial sites.

Q: Will the first clinical trial be limited to the U.S.? Can participants living outside the U.S. participate in the trial?
A: The first clinical trial will be limited to sites within the U.S. Participants and caregivers will be expected to attend regular visits in person throughout the five-year duration of the trial. For this reason, clinical trial participants must be permanent legal residents of the U.S., residing full-time in the U.S. Once safety and efficacy are established in U.S. clinical trials, we plan to expand outside the U.S.

Q: Where are the clinical trial sites?
A: The Seaver Autism Center at Mount Sinai in New York, Rush University in Chicago, and Boston Children's Hospital in Boston are participating in the first-in-human study. Up-to-date study details on ClinicalTrials.gov are posted here: Study Details | JAG201 Gene Therapy Study in Children & Adults with SHANK3 Haploinsufficiency | ClinicalTrials.gov.

We encourage families with children with PMS aged 12 to 36 months who have interest in the JAG201 clinical trial to explore enrolling in a Phelan-McDermid syndrome natural history study. The Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai in New York City, Rush University in Chicago and Boston Children's Hospital in Boston are actively enrolling patients aged 12 to 36 months.

PMS Natural History Study-specific questions may be directed to:

- Seaver Autism Center at Mount Sinai
  New York, New York, United States, 10029
  Contact: Joyce Haddad
  Email: joyce.haddad@mssm.edu
  Currently enrolling ages 12-36 months

- Rush University
  Chicago, Illinois, United States, 60612
  Contact: Lizzy Fitts
  Email: Elizabeth_L_Fitts@rush.edu
  Currently enrolling ages 12-36 months

- Boston Children's Hospital
  Boston, Massachusetts, United States, 02115
  Contact: Anna Cronin
  Email: anna.cronin@childrens.harvard.edu
  Currently enrolling ages 12-36 months

Note that travel stipends may be available for participants in PMS natural history studies at Mount Sinai, Rush University and Boston Children's Hospital, including the Developmental Synaptopathies Consortium (DSC) natural history study. Please inquire with the Phelan-McDermid Syndrome Foundation.

As a reminder, participation in the developmental milestone study does not provide preferential access to clinical trials or gene therapy, and it does not affect eligibility for future trials.

Q: What are the inclusion and exclusion criteria for the trial?
A: Up-to-date study details, including inclusion and exclusion criteria, are available on ClinicalTrials.gov here: Study Details | JAG201 Gene Therapy Study in Children & Adults with SHANK3 Haploinsufficiency | ClinicalTrials.gov. Our first clinical trial for JAG201 will be a small study and includes very specific inclusion and exclusion criteria to meet the guidance set forth by the FDA for Phase 1 clinical trials and to ensure we can appropriately evaluate the safety, tolerance and dose of JAG201.

Generally speaking, the first cohort of participants (first three participants enrolled in the study) were prioritized by age with the youngest eligible participants given preference. We are prioritizing age because we believe treating individuals that are still actively undergoing development may provide greater potential for evaluating the benefit of JAG201.

Throughout the clinical phase of the JAG201 program, our goal remains to demonstrate safety, tolerability, dose and efficacy so the therapy can be considered for approval by the FDA and potentially made available to all individuals with *SHANK3* haploinsufficiency. We are dedicated to doing this as rapidly and as safely as possible.

Q: If my child has a specific medical condition or device (e.g., seizures, ventricular shunt), will it prohibit him/her from participating in the initial clinical trial?
A: Up-to-date study details, including key inclusion and exclusion criteria, are available on ClinicalTrials.gov here: Study Details | JAG201 Gene Therapy Study in Children & Adults with SHANK3 Haploinsufficiency | ClinicalTrials.gov. Our first clinical trial for JAG201 will be a small study and includes very specific inclusion and exclusion criteria to meet the guidance set forth by the FDA for Phase 1 clinical trials and to ensure we can appropriately evaluate the safety, tolerance and dose of JAG201.

Q: Does an immune response to AAV9 prohibit an individual from participating in the initial clinical trial?
A: Up-to-date study details, including key inclusion and exclusion criteria, are available on ClinicalTrials.gov here: Study Details | JAG201 Gene Therapy Study in Children & Adults with SHANK3 Haploinsufficiency | ClinicalTrials.gov. AAV9 immunity is not an exclusion criterion for participation in the clinical study.

Q: Will you be studying JAG201 in both adult and pediatric patients?
A: Our goal is for JAG201 to be studied in both adult and pediatric patients.

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Q: Why have you decided to start the first-in-human trial with pediatric patients instead of adults?
A: Our preclinical data suggest the administration of the gene therapy early in life may provide a greater opportunity for potential benefit. Physicians with expertise in Phelan-McDermid syndrome believe that intervening earlier in a patient's course of illness may help address the underlying deficits caused by the *SHANK3* deficiency while individuals are still actively undergoing development. Accordingly, this initial clinical study is focused on pediatric patients. Results from the initial study will help inform whether JAG201 may be evaluated in broader patient populations in the future.

Q: Does this mean you don't believe treatment with JAG201 will have a benefit in adults?
A: JAG201 may have the potential for benefit in both pediatric and adult patients, but this has not yet been established. The initial clinical study is focused on pediatric patients based on the scientific and clinical rationale for earlier intervention. Results from the initial clinical study will help inform further development of JAG201.

Q: When will you begin dosing adults in the clinical trial?
A: We don't know exactly when adults could be dosed as part of the clinical trial. Timing will depend on when pediatric patients are dosed and data from those trial participants can be evaluated. Based on outcomes and learnings from these first patients, Jaguar may consider dosing adults in a future portion of the clinical trial, potentially as early as 2027.

Q: You have said you will be including pediatric individuals with small deletions and loss-of-function mutations in the initial clinical trial. Can you be more specific about the size of deletions and the kinds of mutations?
A: Up-to-date study details, including inclusion and exclusion criteria, are available on ClinicalTrials.gov here: Study Details | JAG201 Gene Therapy Study in Children & Adults with SHANK3 Haploinsufficiency | ClinicalTrials.gov. The JAG201 clinical trial will enroll patients with a molecular confirmation of a loss of function mutation in *SHANK3* or a class I deletion in 22q13.3 which is characterized by deletion of *SHANK3* or *SHANK3* in combination with *ARSA* and/or *ACR* and *RABL2B*.

Q: How is a class 1 deletion defined?
Class 1 deletions include only *SHANK3* or *SHANK3* in combination with *ARSA* and/or *ACR* and *RABL2B*.

Q: Will JAG201 help those with larger deletions or other mutations not included in the initial clinical trial? What about a ring chromosome?
A: We believe JAG201 has the potential for benefit in all patients with *SHANK3* haploinsufficiency. JAG201 is intended to address SHANK3 haploinsufficiency by delivering a functional *SHANK3* minigene. The potential effect of JAG201 in individuals with larger deletions, other mutations, or a ring chromosome has not yet been evaluated. Results from the initial clinical study will help inform further development of JAG201.

Q: Will trial participants need to stop their ongoing medications during the trial?
A: In general, participants will be allowed to continue maintenance medications as long as they are on a stable dose for the three months leading into the trial.

Q: Will trial participants need to change (i.e., discontinue, decrease or increase) their ongoing therapy services (e.g., ABA, speech, occupational, etc.) during the trial?
A: No. Participants will be allowed to continue in ongoing therapy services. The level of intervention must remain stable for at least three months prior to the start of the trial.

Q: How often will trial participants need to travel to the trial site?
A: Participants and caregivers will be expected to attend regular visits in person throughout the five-year duration of the trial. Visits will be more frequent earlier in the trial and less frequent after the first year.

Q: Are travel expenses for clinical trial participation reimbursed?
A: Yes. A travel expense program is offered to all participants for reimbursement by Jaguar.

Q: If someone participates in a clinical trial for JAG201, will they be excluded from other future clinical trials?
A: Unfortunately, we do not know the answer to this. It would depend on the goals of future clinical trials and the associated investigational therapies as well as applicable regulatory guidance. We can tell you that AAV9 exposure may lead to development of immune system recognition of the AAV vector that could make future treatment with AAV9 unsafe or ineffective.

Q: If my child participates in another clinical trial, for example Neuren's clinical trial, can he/she participate in the JAG201 clinical trial?
A: Generally speaking, sponsors exclude participants who have received or are receiving potentially disease-modifying investigational therapies from clinical trials evaluating new potential treatments. Doing so reduces the possibility of confounding factors when an investigational medicine is being evaluated by regulatory authorities. In other words, excluding exposure to other investigational treatments gives regulatory authorities the confidence that any benefit (or adverse effect) is being caused by the therapy being evaluated and not another medicine. To that end, those who have received or are receiving potentially disease-modifying treatments (including Neuren's NNZ-2591) will not be able to participate in JAG201 clinical trials. This approach gives investigational treatments the opportunity to be thoroughly and appropriately reviewed by regulatory authorities.

If JAG201 is approved, its use in conjunction with other treatments or potential medicines may be possible, and data collected during the clinical trial phase of JAG201 will help inform that possibility.

Q: Is there a possibility that in the future, those who have received or are receiving potentially disease-modifying investigational therapies will be allowed to participate in JAG201 clinical trials?
A: During the clinical phase of the JAG201 program, our goal is to evaluate the safety, tolerability, dose and potential efficacy of JAG201. Eligibility criteria may evolve as more data become available. However, individuals who have received or are receiving potentially disease-modifying investigational therapies are not expected to be eligible for the initial JAG201 clinical trial because prior or concurrent investigational treatment could make it difficult to interpret safety and efficacy data.

If JAG201 is approved, its use in conjunction with other treatments or potential medicines may be possible, and data collected during the clinical trial phase of JAG201 will help inform that possibility.

Q: If my child is not selected for enrollment in the initial clinical trial, does that also mean they cannot participate in any potential future trials for JAG201?
A: We do not know the specific inclusion/exclusion criteria for any potential future clinical trials of JAG201, however, not meeting criteria in the initial trial does not immediately exclude someone from participating in any potential future trials.

Q: If my child is not selected for enrollment in the initial clinical trial, can I gain access to JAG201 by some other means (e.g., purchase out of pocket)? What if I assume all liability?
A: JAG201 is an investigational gene therapy. At this time, JAG201 is only accessible through clinical trial participation.

JAG201 First-in-human Clinical Trial Progress Questions

Q: Have any patients been dosed in the JAG201 initial clinical trial?
A: Yes, seven pediatric patients have been dosed with JAG201 in the initial clinical trial. Dosing of Cohort 1 is complete with the first three patients having received the starting dose of JAG201. Participants in Cohort 2 received an escalated dose of JAG201. As of the date this FAQ was released (July 8, 2026), no treatment-related serious adverse events (SAE) have been observed. We look forward to providing additional updates as the trial progresses.

Q: Have any serious safety concerns been observed in any patients dosed with JAG201?
A: As of the date this FAQ was released (July 8, 2026), no treatment-related SAEs have emerged.

Q: Does the treatment appear to be working in any patients dosed with JAG201?
A: Early indications of clinical benefit have been observed across neurodevelopmental domains, including communication, motor, cognitive and social. We look forward to the complete data set from the first-in-human trial to be able to determine any possible efficacy of JAG201.

Q: Where have patients been dosed with JAG201?
A: Patients have been dosed with JAG201 at the Seaver Autism Center at Mt. Sinai in New York, at Rush University Medical Center in Chicago and at Boston Children's Hospital in Boston.

Q: When will subsequent trial participants be dosed with JAG201?
A: JAG201 will be evaluated in humans for the first time in this initial clinical study. Although the starting dose is supported by preclinical studies in animals, we plan to dose one patient at a time to allow for thorough safety evaluations of individual patients. If no safety concern is identified in the first patient's safety data, then dosing of the next patient can proceed. This approach is not unusual in early-stage gene therapy clinical trials, particularly for the first few patients that receive a particular dose. It allows a Sponsor (in this case, Jaguar) and the United States Food and Drug Administration (FDA) to review safety information and make necessary adjustments to the clinical trial and dosing of subsequent patients if a safety concern arises.

Q: When will dosing be completed for all first-in-human clinical trial participants?
A: We anticipate target enrollment and dosing to be completed in Cohort 2 of the first-in-human trial in H2 of 2026.

JAG201 Future Clinical Trials Questions

Q: When will the next phase of clinical trials begin?
A: The current trial serves as a Phase 1/2 trial. Jaguar is aiming to conduct a registrational phase trial next, in which the emerging data could support an application for approval of JAG201 with the FDA.

Jaguar is required to engage with the FDA to gain approval for beginning a registration phase clinical trial. Data from participants in the two dosing cohorts must be available for the engagement with regulators. The earliest Jaguar may be able to start a registration trial would be in 2027.

Q: Will the same eligibility criteria used for the current first-in-human trial be used for the registrational phase clinical trial?
A: Throughout the clinical phase of the JAG201 program, our goal is to evaluate the safety, tolerability, dose and potential efficacy of JAG201.

The eligibility criteria for the registrational phase clinical trial that will follow the current first-in-human trial of JAG201 has not yet been determined. Jaguar will be working with the FDA to determine criteria for potential approval of JAG201, which will be the basis of the eligibility criteria for a future registrational phase clinical trial. It is possible the inclusion criteria, including age and genetics, will be different for the registrational phase clinical trial.

Q: What ages will be eligible to participate in the next phase of clinical trials for JAG201?
A: The eligibility criteria for the registrational phase clinical trial that will follow the current first-in-human trial of JAG201 has not yet been determined. Jaguar will be working with the FDA to determine criteria for potential approval of JAG201, which will be the basis of the eligibility criteria for a future registrational phase clinical trial. It is possible the inclusion criteria, including age and genetics, will be different for the registrational phase clinical trial.

Q: How many trial participants do you plan to enroll in the next phase of clinical trials for JAG201?
A: The number of participants in the registrational phase clinical trial for JAG201 has not yet been determined. Jaguar will be working with the FDA to determine criteria for potential approval of JAG201, which will inform the eligibility criteria and number of participants for a future registrational phase clinical trial. It is possible the inclusion criteria, including age and genetics, will be different for the registrational phase clinical trial.

Q: When will JAG201 be approved in the United States?
A: JAG201 is an investigational gene therapy. We cannot speculate as to if or when JAG201 may be approved by the FDA. To learn more about the drug development process in the United States, you can visit https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process.

JAG201 Activities Outside the U.S. Questions

Q: Do you have any clinical trial applications for JAG201 with MHRA, EMA or other regulatory bodies outside the U.S.?
A: Having received IND clearance from the FDA, we are currently in the process of enrolling our first clinical trial in the U.S. No additional expansion is being planned at this time as we prioritize our regulatory pathway in the U.S.

Our aim is to make JAG201 available as broadly as possible to individuals with PMS, if it is shown to be safe and effective and receives regulatory approval. One possible approach would be to use U.S. registrational data, after a potential U.S. approval, to support submissions to regulatory authorities outside the U.S. This has been successfully accomplished with other approved treatments in various diseases.

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JAG201 Manufacturing Questions

Q: I saw that Jaguar announced it has partnered with Andelyn Biosciences for manufacturing support. Can you explain what Andelyn Biosciences will be doing for the JAG201 program?

A: Andelyn Biosciences is a contract development and manufacturing organization and will provide late-stage clinical and Process Performance Qualification (PPQ) manufacturing of JAG201. This means the company will produce the JAG201 drug substance for late-stage clinical trial supply and as part of the validation phase required by the FDA before commercial manufacturing begins.

Genetic Testing Questions

Q: Can you recommend a site/company/physician/lab for my loved one to be tested for a *SHANK3* gene mutation or deletion?

A: We are not in a position to recommend care or testing for your loved one. We encourage you to speak with your loved one's health care provider to discuss potential genetic testing options.

Q: What genetic test does my loved one need to determine if he/she has *SHANK3* mutation or deletion?

A: Examples of genetic tests that can diagnose both mutations and deletions include whole genome sequencing, whole exome sequencing, chromosomal microarray (CMA) and genetic panels that sequence the *SHANK3* gene**.** It is important to note that not all types of genetic testing are the same. For example, CMA can miss smaller deletions or sequence variants in *SHANK3*, leading to missed or false negative diagnoses.[2] If your loved one's prior genetic test yielded a non-diagnostic result, more advanced techniques like exome and genome sequencing may be able to detect an underlying *SHANK3* variant. We encourage you to speak with your loved one's health care provider to discuss potential genetic testing options.

Q: Does Jaguar participate in a *SHANK3* genetic testing partnership program?

A: Yes. Jaguar is partnering with GeneDx on the *Autism Answers: SHANK3 Inform Partnership Program* to provide eligible individuals who meet specific criteria with access to exome and genome sequencing. Individuals with moderate to severe development delay, intellectual disability, autism spectrum disorder (ASD), or autistic-like behavior with clinical suspicion of Phelan-McDermid syndrome will have access to sequencing from GeneDx, with costs covered by Jaguar Gene Therapy when patients have Medicare / Medicare Advantage and when commercial insurance coverage is unavailable.

Q: Is the *Autism Answers: SHANK3 Inform Partnership Program* available now?

A: Yes. If you are interested in learning more about the program, talk with your healthcare provider and direct them to https://www.genedx.com/genetic-testing-program/shank3/.

Q: What are the eligibility criteria for participating in *Autism Answers: SHANK3 Inform Partnership Program*?

A: To be eligible for the program, patients must meet certain criteria, including the following:

- Patient must reside in the United States;

[2] Srivastava S, Cole J, Cohen J, et al. Survey of the Landscape of Society Practice Guidelines for Genetic Testing of Neurodeve lopmental Disorders. Ann Neurol. 2024 Nov;96(5):900-913. doi: 10.1002/ana.27045.

- Patient's ordering provider must be authorized under applicable law to order genetic testing in the United States;
- Patient must present with moderate to severe development delay, intellectual disability, ASD, or autistic-like behavior with clinical suspicion of Phelan-McDermid syndrome; and
- Have not had prior genetic testing performed by a clinical laboratory that resulted in a confirmed diagnosis of Phelan-McDermid syndrome (*SHANK3* haploinsufficiency).

Additional eligibility criteria apply and can be discussed with your health care provider.

Q: How can someone participate in the *Autism Answers: SHANK3 Inform Partnership Program*?
A: Begin by speaking with a health care provider about taking advantage of the program and direct them to https://www.genedx.com/genetic-testing-program/shank3/. Note – this program is only available for those who have not had prior genetic testing that resulted in a confirmed genetic diagnosis of *SHANK3* haploinsufficiency.

Q: Are costs covered for those who participate in the *Autism Answers: SHANK3 Inform Partnership Program*?
A: The *Autism Answers: SHANK3 Inform Partnership Program* will utilize commercial insurance to help cover costs of the genetic testing when available. In some cases, this may require an individual with commercial insurance to pay a co-pay. When commercial insurance coverage is unavailable or when patients have Medicare or Medicare Advantage, Jaguar will cover the costs.

Regulatory Questions

Q: What is Rare Pediatric Disease designation, and why is it important?
A: The FDA grants Rare Pediatric Disease designation for serious and life-threatening rare pediatric diseases. Under this program, companies are eligible to receive a priority review voucher for a subsequent marketing application for a different product following approval of a product with rare pediatric disease designation. The priority review voucher may be used by the sponsor or sold or transferred. This program is meant to stimulate drug development for rare pediatric diseases.

Q: What is Fast Track designation, and why is it important?
A: The Fast Track program is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to patients earlier. Fast Track addresses a broad range of serious conditions. A therapy that receives Fast Track designation is eligible for more frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval, among other benefits.

Q: What is Orphan Drug Designation, and why is it important?
A: The Orphan Drug designation is for therapies that show promise in the treatment, prevention or diagnosis of orphan diseases. An orphan disease is a rare disease or condition that affects fewer than 200,000 people in the United States. The Food and Drug Administration (FDA) created the Orphan Drug Act to encourage and provide special incentives to companies that undertake the development of orphan drugs.

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