



**About Taysha’s investigational gene therapy for Rett syndrome (TSHA-102):**

- What is the underlying cause of Rett syndrome?
  - In most patients with Rett syndrome, there is a mutation in *MECP2*, which is a gene that tells cells how to make a protein called Methyl-CpG-binding protein 2 (MeCP2)
  - This protein plays an important part in the development of the brain throughout childhood by maintaining normal brain function and communicating between nerve cells
  - In Rett patients with a *MECP2* gene mutation, the body does not make enough MeCP2 or produces abnormal MeCP2
- What is Taysha’s investigational approach to gene therapy for Rett syndrome?
  - Taysha’s investigational gene therapy product, TSHA-102, is designed to deliver a working copy of the *MECP2* gene to the affected cells
  - TSHA-102 uses a novel technology called miRARE, developed by Dr. Sarah Sinnet and Dr. Steven Gray of UT Southwestern Medical Center
  - The clinical trials will determine whether the working copy of the *MECP2* gene can be packaged with our miRARE technology to safely control the level of MeCP2 protein expression
- How is Taysha’s investigational gene therapy delivered?
  - The working *MECP2* gene is inserted into a delivery vehicle, called a vector, which is then injected intrathecally, into the spinal fluid in the lower back (lumbar region)
  - From there, the gene therapy is carried throughout the spinal cord and brain so that it can be transferred into the cells that need them
- What delivery vehicle is used to transfer the *MECP2* gene?
  - The vector that Taysha uses is an adeno-associated virus (AAV9) viral vector that is not known to cause disease in humans
  - AAV9 is a commonly used vector, which has been used in other investigational and approved gene therapies

If you have questions or would like to connect with a member of our team, please contact [medinfo@tayshagtx.com](mailto:medinfo@tayshagtx.com).

As always, we are grateful for the continued support of the Rett syndrome community and the Rett patient advocacy organizations. It is a privilege to partner with you. Your continued input helps to shape the work that we do and allows us to move as quickly as possible.

We look forward to providing further updates as new information becomes publicly available.

Sincerely,  
The Taysha Patient Affairs Team

