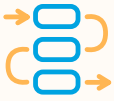
The Development of TSHA-102

A look at progress to date– and the road ahead

Taysha GENE THERAPIES

TSHA-102 reflects years of progress

Developing a potential new treatment takes **time, care, and the dedication** of researchers, clinicians, advocacy organizations, and families all working together.



A gene therapy like TSHA-102 can take 10–20 years or longer to go from scientific discovery to potential Food and Drug Administration (FDA) approval.[1-4]

This timeline was created to help you understand the steps and progress of **TSHA-102**—what's been completed, where we are today, and what may come next

Scientific beginnings & discovery

Scientists studied Rett syndrome to understand how it affects the body and uncovered the gene behind the condition.

1966

Andreas Rett publishes the first clinical description of Rett syndrome[5]

1999

Huda Zoghbi discovers that ***MECP2* mutations cause most Rett syndrome cases**[6]

2000s

Scientists learn that mutations in the *MECP2* gene can lead to too little or too much MeCP2 protein in the body[5]

- Too little MeCP2 protein can cause Rett syndrome
- Too much MeCP2 protein can also be harmful

Building gene therapy for Rett syndrome

Researchers began exploring how gene therapy may help address the underlying cause of Rett syndrome.

2008–2013

Early gene therapy approaches explored in the lab[7-9]

2014

Rett Syndrome Research Trust launches Gene Therapy Consortium to advance gene and cell research[10]

~2017–2020

- Creation of **mini*MECP2***, led by Sir Adrian Bird[11-14]
- Creation of **miRARE**, led by Steven Gray and Sarah Sinnett[11-14]*

Advancing new approaches: TSHA-102

Developed from years of scientific discovery, TSHA-102 moves to preclinical testing, an important step on the path toward clinical trials in humans.[7-9,11,14,15]

*Early seed funding came from Rett Syndrome Research Trust.

Initial testing of TSHA-102

TSHA-102 was tested in the lab and in animal models to better understand how it works and to help confirm it could be safely studied in humans.[14,16]

2021-2022

Researchers studied **TSHA-102** in animals (eg, mice and non-human primates) to understand safety, how well it works, how it moves through and reaches different parts of the brain, and to find the right dose. Using multiple animal models provided a thorough and reliable understanding before moving forward[14,17]

2021

Manufacturing processes are developed to prepare the therapy for clinical trials[17]

Prepping for clinical trials

After vigorous research and testing, Taysha submitted an Investigational New Drug (IND) application to the FDA to ask for permission to begin studying **TSHA-102** in humans.[18]

2022

A first-in-human study application was submitted to regulators and accepted[19,20]

Moving toward potential approval

Researchers begin studying **TSHA-102** in people to learn more about its safety, dosing, and potential benefits.[20]

2023-2025

REVEAL Phase 1/2 Studies (Part A) of **TSHA-102** begins, marking the first time **TSHA-102** is studied in people with Rett syndrome[20-22]

2025

REVEAL Pivotal Study (Part B) starts[22]

2025-2026

The manufacturing process that will be used to produce **TSHA-102** at a larger scale was developed and confirmed. This is an essential step for approval, ensuring the gene therapy can be made safely, consistently, and at the same high quality for all patients[23-26]

2026

- 12-month interim results available from the **REVEAL Phase 1/2 Studies (Part A)**[27]
- Dosing complete in the **REVEAL Pivotal Study (Part B)**[27]
- Dosing complete in the **ASPIRE Study**[27]

Continuing the progress

The safety and potential benefits of **TSHA-102** are continuing to be studied in humans who received the investigational gene therapy.[28,29]

2026 and beyond

Participants from the **REVEAL** and **ASPIRE Studies** will be followed for 4+ years after receiving **TSHA-102**[28,29]

REVEAL
PHASE 1/2 STUDIES
RETT SYNDROME

REVEAL Phase 1/2 (Part A)

A first-in-human study evaluating the safety, tolerability, and potential benefits of **TSHA-102** at two dose levels in girls and young women (aged 6 to 21) living with Rett syndrome[20]

REVEAL
RETT SYNDROME
PIVOTAL STUDY

REVEAL Pivotal (Part B)

A Phase 3 clinical trial studying potential benefits and safety of **TSHA-102** at the selected dose in girls and young women (aged 6 to 21) with Rett syndrome. The data collected in this study will help regulators to decide if **TSHA-102** can be approved for patients[28]

ASPIRE
PHASE 2b/3 STUDY
RETT SYNDROME

ASPIRE

An open-label study evaluating the safety and potential benefits of **TSHA-102** in young girls (aged 2 to 3) with Rett syndrome[29]

Learn about what's next for TSHA-102.

From clinical studies to potential FDA approval

What's next for TSHA-102

1 Follow-up and data collection

After receiving **TSHA-102** in a clinical trial, participants will be followed for several years.[28,29]

Collecting this information is important because it helps track **whether TSHA-102 continues to work safely and effectively** for patients over a longer amount of time.[28,29]

2 Making sense of the data

Researchers will carefully review the results collected from these follow-ups to make sure everything is **complete and accurate.**[30]

Taysha has aligned with the FDA on an interim analysis at the 6-month time point of the REVEAL Pivotal Study. The main study results are measured at 12 months, but this earlier analysis may help create a faster path to approval.[22,31]

3 Regulatory review

If the clinical trial results support the safety and efficacy of **TSHA-102**, Taysha will submit a **Biologics License Application (BLA)** to the FDA.

BLA acceptance

The FDA decides if it will **accept** the application for filing and begin review within 60 days.[32]

FDA review

The FDA will thoroughly review the **efficacy and safety data** for **TSHA-102**. It will also look at how the treatment is made and may ask to **inspect the manufacturing facility**. If needed, the FDA may request additional information from Taysha.[25,33]

If **TSHA-102** qualifies for a **Priority Review**, the FDA will review the application in 6 months from the filing date versus the standard 10 months. This designation is given to therapies that, if approved, would significantly improve the treatment of a serious condition.[32]

Did you know?

TSHA-102 has special FDA designations for rare pediatric diseases, breakthrough treatments, and regenerative medicine, meaning it could get extra support and faster review time to help make **TSHA-102** available to families sooner.[22,34]

4 FDA approval decision

The FDA will make the final decision on whether to approve **TSHA-102** for use in individuals living with Rett syndrome.[33]

Decades of research, supported by organizations like the **International Rett Syndrome Foundation** and the **Rett Syndrome Research Trust**, along with the dedication of **scientists**, the support of **families** living with Rett syndrome, and the courage of **those who have participated in clinical trials**, have made the progress of **TSHA-102** possible.

International Rett Syndrome Foundation
www.rettsyndrome.org

RETT SYNDROME RESEARCH TRUST

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We understand that for families living with Rett syndrome, every day matters

Taysha is committed to moving this investigational gene therapy forward with **urgency and care**, so it may be a treatment option as **quickly and safely** as possible.

Click the link to sign up for updates on TSHA-102 at tayshagtx.com

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