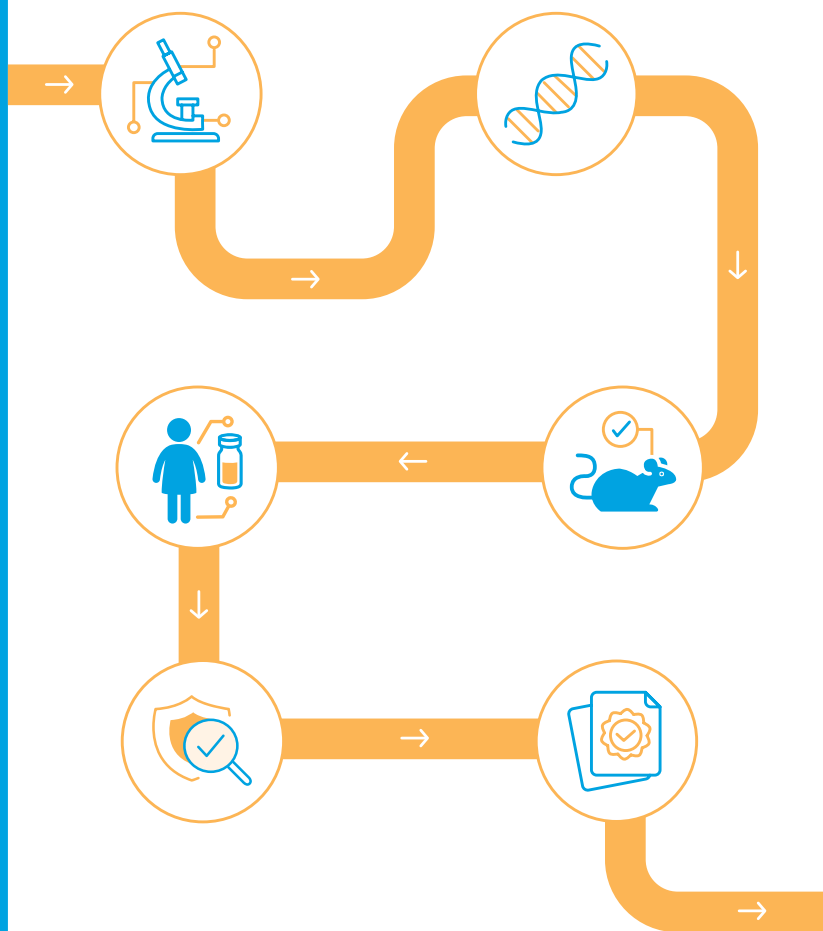


The Development of TSHA-102

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

**1**

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 syndrome⁵

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 body⁵

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



**2**

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 lab⁷⁻⁹

2014

Rett Syndrome Research Trust launches Gene Therapy Consortium to advance gene and cell research¹⁰

~2017-2020

- Creation of **miniMECP2**, led by Sir Adrian Bird¹¹⁻¹⁴
- Creation of **miRARE**, led by Steven Gray and Sarah Sinnett^{11-14*}
- Taysha Gene Therapies founded, licensed the Rett syndrome gene therapy program and launched development of **TSHA-102**^{12,15}

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.^{7-9,11,14,16}

*Early seed funding came from Rett Syndrome Research Trust.



**3**

Pre-clinical testing of TSHA-102

TSHA-102 was extensively tested in the lab and in animal models to evaluate how it works and to help confirm it could be safely studied in humans.^{14,17,18}

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^{14,19}

2021

Manufacturing processes are developed to prepare the therapy for clinical trials¹⁹

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^{20,21}

**4**

Moving toward potential approval

Researchers begin studying **TSHA-102** in people to learn more about its safety, dosing and potential benefits.²¹

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 syndrome²¹⁻²³

2025

REVEAL Pivotal Study (Part B) starts²³

2025-2026

The manufacturing process for larger-scale production of **TSHA-102** was developed—an essential step toward approval that ensures the gene therapy can be made safely, consistently and at high quality for all patients.²⁴⁻²⁷

2026

- 12-month interim results available from the **REVEAL Phase 1/2 Studies (Part A)**²⁸
- Dosing complete in the **REVEAL Pivotal Study (Part B)**²⁸
- Dosing complete in the **ASPIRE Study**²⁸

**5**

Continuing to monitor progress

The safety and potential benefits of **TSHA-102** are continuing to be studied in humans who received the investigational gene therapy. The complete clinical trial dataset will ultimately be provided to the FDA for review.^{29,30}

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 2 dose levels in girls and young women (aged 6 to 21) living with Rett syndrome²¹

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 patients³⁰

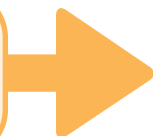
ASPIRE

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 syndrome²⁹

Learn about what's next
for TSHA-102.





6

From clinical studies to
potential FDA approval

What's next for TSHA-102

Follow-up and data collection



After receiving **TSHA-102** in a clinical trial, patients may be monitored for 4+ years after treatment.^{28,29}

Collecting this information is important to better understand the long-term safety and durability of **TSHA-102**, even if the therapy is FDA approved.^{29,30}

Making sense of the data



Researchers will carefully review the results collected from these follow-ups to make sure everything is **complete and accurate**.³¹

Taysha has aligned with the FDA to conduct an interim analysis of the REVEAL Pivotal Study after all participants have reached the 6-month follow-up time point. The main study results are measured at 12 months, but this earlier analysis may help create a faster path to approval.^{23,32}



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.³³



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.^{26,34}



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.³³



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.^{23,35}

FDA approval decision



The FDA will make the final decision on whether to approve **TSHA-102** for use in individuals living with Rett syndrome.³⁴

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®



RETT
SYNDROME
RESEARCH
TRUST



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Taysha is committed to moving its investigational gene therapy forward with urgency and care

Our goal is to make **TSHA-102** 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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