

The Road to RETHYMIC

Helping you and your family navigate the different steps of the congenital athymia treatment journey, from diagnosis to receiving RETHYMIC and beyond.

RETHYMIC is the first and only FDA-approved tissue-based treatment for congenital athymia. It is engineered to help children develop an immune system sufficient to fight infections.^{1,2}

Indication

RETHYMIC® (allogeneic processed thymus tissue–agdc) is indicated for immune reconstitution in pediatric patients with congenital athymia.

RETHYMIC is not for use in patients who have been diagnosed with severe combined immunodeficiency (SCID).

Select Safety Information

Infection Control: Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC. Immune reconstitution is needed for the body to produce cells in the immune system to fight infection. Your child's doctor should advise you of infection control measures which should be followed immediately after treatment and until the immune system starts working at a sufficient level. Monitor your child closely for signs of infection, including fever. Your child should be maintained on immunoglobulin replacement and prophylactic antimicrobials until certain criteria are met as determined by your doctor.

Please see additional Important Safety Information on page 9, and the full [Prescribing Information](#).

 **RETHYMIC**®
allogeneic processed
thymus tissue–agdc



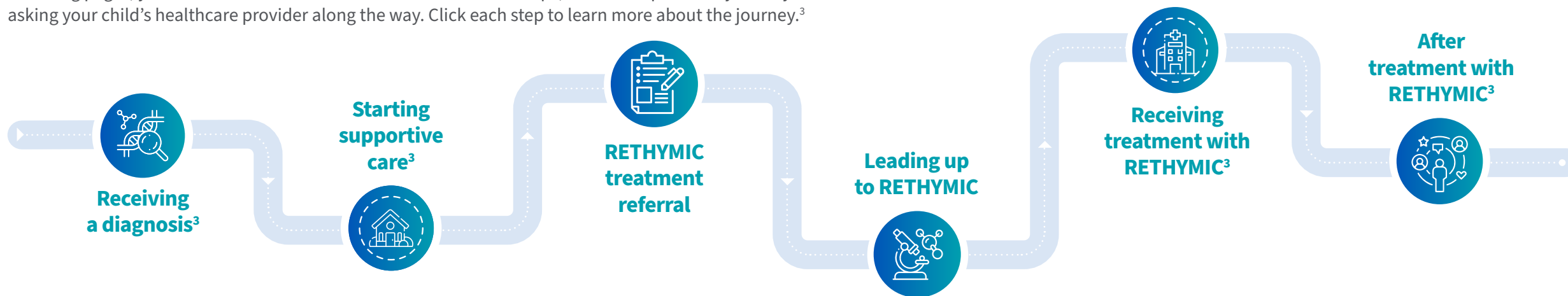
Jada, a child with
congenital athymia.



The congenital athymia treatment journey



There are several key steps that happen along your child's journey with congenital athymia, from diagnosis to the period after they receive treatment with RETHYMIC. While each family's journey may be different, on the following pages, you'll find more information about each of these steps, as well as questions you may consider asking your child's healthcare provider along the way. Click each step to learn more about the journey.³



ENZYVANT
CONNECT

Consider speaking to your child's healthcare provider about enrolling in our patient support program, Enzyvant CONNECT®, to access support and exclusive resources for different milestones throughout your family's journey with congenital athymia. Some of these program offerings are noted on the following pages.

Enzyvant CONNECT is available to all patients with any type of insurance—including commercial plans, Medicare, or Medicaid—as well as patients who are underinsured or have no insurance coverage.

[Learn more](#)

Select Safety Information

Graft versus Host Disease (GVHD): RETHYMIC may cause or make pre-existing GVHD worse. Your child will be monitored for GVHD and treated if needed. Symptoms of GVHD may include fever, rash, enlarged lymph nodes, inflammation of the gastrointestinal system and/or diarrhea.

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Receiving a diagnosis

Congenital athymia is often detected through newborn screening for severe combined immunodeficiency (SCID), a test that is required in all 50 states in the US.⁴



Congenital athymia vs SCID

While these two conditions are not the same, the test for SCID will likely indicate to your child's healthcare provider that further testing and examination are needed.⁴

After a positive screening result, an immunologist will use a laboratory technique called flow cytometry to verify low T cells and possibly lead to a diagnosis of congenital athymia.⁴



Additional testing

Prenatal testing may detect genetic abnormalities that are associated with congenital athymia, but congenital athymia is usually not detected until birth.^{4,5}

Your child's healthcare provider may also test for additional underlying rare syndromes or genetic conditions.⁴

Resources that may help:



Understanding and Living With Congenital Athymia

A guide to congenital athymia, from diagnosis to creating a care plan.

Questions to ask your child's healthcare provider:

- What are the immediate next steps my family will need to take after my child is diagnosed?

Select Safety Information

Autoimmune Disorders: Autoimmune-related adverse events occurred in patients treated with RETHYMIC. These events included: low platelets, low white blood cells, protein in urine, low red blood cells, hair loss, poor thyroid function, inflammation of liver, inflammation of the joints, inflammation of the spinal cord, loss of pigment in the skin, eyes and hair, overactive thyroid function, and loss of function of the ovaries. Your doctor will monitor your child regularly including performing blood tests.

Please see additional Important Safety Information on page 9, and the full [Prescribing Information](#).



Starting supportive care

Once a diagnosis of congenital athymia has been confirmed, your child's healthcare provider may recommend various precautionary measures you and your family can take—both in the hospital and in the home.³

Supportive care

Every family's care plan may be different, but it most likely won't be easy. It is recommended that any precautionary measures should be followed throughout your family's journey until your child has received treatment with RETHYMIC and their healthcare provider has determined that the measures can be lifted.^{3,4}

After diagnosis, your child's healthcare provider may:



Recommend strict isolation for everyone in your household and restricting visitors⁴



Instruct the mother to stop breastfeeding to prevent potentially transmitting viruses, particularly cytomegalovirus⁴



Start your child on preventative treatments⁴



Not administer any vaccines³

Your child's healthcare provider may recommend additional precautionary measures you can take in your home.

[Explore supportive care](#)

Select Safety Information

Kidney Disease: Treatment with RETHYMIC is a risk factor for death in patients with pre-existing kidney disease.

Please see additional Important Safety Information on page 9, and the full [Prescribing Information](#).



Resources from Enzyvant CONNECT:



Your Congenital Athymia Medical Log

A tool for tracking your child's medications, appointments, and lab results

Discussing Congenital Athymia

Helping friends and family understand your child's condition

Questions to ask your child's healthcare provider:

- What are some of the visitation restrictions that should be put in place in my home?
- Are there ways my friends and relatives outside of my immediate family can support us?
- Will my child need to stay in the hospital or can they live at home?
- How often will my child need to see their care team or healthcare providers?



RETHYMIC treatment referral

RETHYMIC is the first and only FDA-approved tissue-based treatment for congenital athymia. It is engineered to help children develop an immune system sufficient to fight infections.^{1,2}



RETHYMIC is currently only available at Duke University Health System in Durham, North Carolina.⁶



Your child's healthcare provider will need to reach out to Duke University Health System to begin the process of referring them for treatment with RETHYMIC.



This is a good time to discuss enrolling in Enzyvant CONNECT with your child's healthcare provider. A dedicated Support Liaison and Access Specialist can provide you with educational support and financial assistance throughout your journey.

Sumitomo Pharma America, Inc. and Enzyvant CONNECT are not responsible for treatment decisions or timing for treatment.

Select Safety Information

Cytomegalovirus (CMV) Infection: In clinical studies with RETHYMIC, 4 out of 4 patients with pre-existing CMV infection prior to the implantation with RETHYMIC died. Talk to your doctor about the benefits/risks of treatment if your child has pre-existing CMV infection.

Cancer: Due to your child's weakened immune system, there is increased risk of developing certain cancers. Your child's doctor will monitor your child through testing for Epstein-Barr virus (EBV) and cytomegalovirus (CMV), which are two viruses that can cause cancer.

Please see additional Important Safety Information on page 9, and the full [Prescribing Information](#).



Resources that may help:



Enzyvant CONNECT Program Overview

An overview of the patient support program, care team, commercial co-pay program, and exclusive resources



A Caregiver's Guide to RETHYMIC

A guide to help you better understand RETHYMIC. [View it here](#)

Questions to ask your child's healthcare provider:

- How long does it take for RETHYMIC to be made?
- Will you and the rest of the care team continue to see my child after they've been referred for treatment with RETHYMIC?
- How can I enroll in Enzyvant CONNECT? What kind of support does it offer?



Leading up to RETHYMIC

The time leading up to treatment with RETHYMIC may be very difficult, especially when so much is at stake. However, there are a number of factors that will determine when your child may receive treatment.^{4,7}

Unlike a transplant, RETHYMIC is developed for one child at a time through a complex process using donor thymus tissue.^{1,8}



When an infant less than 9 months of age has cardiac surgery, some thymus tissue may need to be removed to access the heart.⁸



With consent of the infant donor's parents or guardian, the thymus tissue is donated to make RETHYMIC.⁸



The infant, their birth mother, and the tissue undergo extensive testing to make sure the donation meets FDA quality and safety standards when engineering RETHYMIC.⁸



Unlike many other medications, RETHYMIC is not an off-the-shelf product.



The tissue from a single pediatric donor allows for the manufacturing of RETHYMIC for one child.¹



The availability of RETHYMIC is dependent on multiple factors, including the size of the thymus tissue that is donated.⁷

Select Safety Information

Transmission of Serious Infections: Because RETHYMIC is made from human tissue, and animal products are used in the manufacturing process, transmission of infectious diseases may occur.

Vaccinations: Your child should not receive any vaccinations until he or she has met certain requirements set by your doctor. Talk to your child's doctor prior to any vaccinations.

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Resources from Enzyvant CONNECT:



CONNECTION to Resources Kit

A kit that provides helpful resources for this step of the journey, including *Sadie's Search*, a storybook written specifically with your child in mind



CONNECT Quarterly

Newsletters and a webinar series featuring educational information for caregivers and activities for the whole family

Questions to ask your child's healthcare provider:

- How can I prepare for my child to receive treatment with RETHYMIC?
- What should my family and I expect in the time leading up to treatment with RETHYMIC?
- Are there any other organizations or communities for people affected by rare diseases or primary immunodeficiencies?



Receiving treatment with RETHYMIC

To receive treatment with RETHYMIC, you and your child will need to travel to Durham, North Carolina.



Administration

RETHYMIC is a one-time treatment administered via a single surgical procedure. The procedure is performed in an in-patient setting, and your child will need to stay in the hospital before the procedure and afterward for observation.^{1,2}



Implantation

Children are put under general anesthesia and RETHYMIC is implanted in one, or both if necessary, of the thighs. The thigh muscle is used because its rich supply of blood provides oxygen and nutrients to RETHYMIC.^{1,3}

Select Safety Information

Anti-HLA Antibodies: Prior to receiving RETHYMIC your child will be tested for HLA antibodies, which are proteins that may be present in your child's blood. If your child has these antibodies, he/she will need to receive RETHYMIC from a donor that does not express those HLA proteins.

HLA Typing: If your child has received a hematopoietic cell transplantation (HCT) or a solid organ transplant, they will have a test to look for specific antibodies that could interfere with the effect of RETHYMIC. If they are present, then it will be necessary to receive RETHYMIC from a certain group of donors that do not have these proteins.



Resources from Enzyvant CONNECT:



Enzyvant CONNECT Arrival Guide

An interactive resource to help you navigate Durham, NC, during your stay

Questions to ask your child's healthcare provider:

- How much time will I have to travel to North Carolina once I'm notified that my child will be treated with RETHYMIC?
- How can my child and I remain isolated when we travel?
- Do you have any recommendations for traveling? What should I pack?
- What type of support is available for families that travel to Durham, NC?

Please see additional Important Safety Information on page 9, and the full [Prescribing Information](#).

Jada, a child with congenital athymia.





After treatment with RETHYMIC

Once your child is discharged from the treatment center, they will travel home and return to the care of their healthcare provider and care team. RETHYMIC needs time to help develop an immune system sufficient to protect from infections, which is unlikely to develop prior to 6 to 12 months after treatment. For some children, it may take up to 2 years.^{1,8}



Continuing precautionary measures

Your child will remain immune compromised while RETHYMIC starts to work, so to keep them safe, life immediately after treatment will have to look very similar to life before it. Careful monitoring and isolation for the whole family are required to ensure your child avoids infection and other complications after treatment.^{1,3,4}

Work with your child's healthcare provider to determine when infection prevention measures can be lifted.^{1,4}

Learn more about the milestones your child will need to reach.

Explore post-treatment care

Select Safety Information

Deaths: 105 children participated in the clinical studies of RETHYMIC. 29 of the patients died, including 23 in the first year after implantation of RETHYMIC.

What are the most common side effects with RETHYMIC?

The most common side effects with RETHYMIC are hypertension (high blood pressure), cytokine release syndrome, rash, hypomagnesemia (low magnesium), renal impairment / failure (decrease of kidney function), thrombocytopenia (low platelets), and graft versus host disease.

These are not all of the possible side effects of RETHYMIC. Talk to your child's doctor about any side effect that bothers your child or does not go away.

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Resources from Enzyvant CONNECT:



Post-treatment Resources

This kit contains a guide to what you can expect after treatment with RETHYMIC, a T-cell tracker to mark your child's progress, and an activity book for the whole family

Questions to ask your child's healthcare provider:

- What are the different markers for immune reconstitution that will be tracked?
- How often will my child's T-cell levels be tested after receiving treatment with RETHYMIC? Where will these tests take place?
- When can my family and I begin to relax strict isolation? When can my child meet other people or go to places outside of our home?
- When can my child receive vaccinations? Are there any vaccines they'll need to avoid?

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These are not all of the possible side effects of RETHYMIC. Talk to your child's doctor about any side effect that bothers your child or does not go away.

You are encouraged to report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

References: **1.** RETHYMIC [package insert]. Marlborough, MA: Sumitomo Pharma America, Inc; 2023. **2.** Enzyvant Therapeutics GmbH. Enzyvant receives FDA approval for RETHYMIC® (allogeneic processed thymus tissue-agdc), a one-time regenerative tissue-based therapy for pediatric congenital athymia. Enzyvant Therapeutics, Inc. October 8, 2021. Accessed March 3, 2023. <https://enzyvant.com/enzyvant-receives-fda-approval-for-rethymic-allogeneic-processed-thymus-tissue-agdc-a-one-time-regenerative-tissue-based-therapy-for-pediatric-congenital-athymia/> **3.** Gupton SE, McCarthy EA, Markert ML. Care of children with DiGeorge before and after cultured thymus tissue implantation. *J Clin Immunol.* 2021;41(5):896-905. doi:10.1007/s10875-021-01044-0 **4.** Collins C, Sharpe E, Silber A, Kulke S, Hsieh EWY. Congenital athymia: genetic etiologies, clinical manifestations, diagnosis, and treatment. *J Clin Immunol.* 2021;41(5):881-895. doi:10.1007/s10875-021-01059-7 **5.** Mustillo PJ, Sullivan KE, Chinn IK, et al. Clinical practice guidelines for the immunological management of chromosome 22q11.2 deletion syndrome and other defects in thymic development. *J Clin Immunol.* 2023;43(2):247-270. doi:10.1007/s10875-022-01418-y **6.** Hsieh EWY, Kim-Chang JJ, Kulke S, Silber A, O'Hara M, Collins C. Defining the clinical, emotional, social, and financial burden of congenital athymia. *Adv Ther.* 2021;38(8):4271-4288. doi:10.1007/s12325-021-01820-9 **7.** Food and Drug Administration. Summary Basis for Regulatory Action. October 8, 2021. BLA STN: 125685/0 **8.** Markert ML, McCarthy EA, Gupton SE, Lim AP. Cultured thymus tissue transplantation. In: Sullivan KE, Stiehm ER, eds. *Stiehm's Immune Deficiencies: Inborn Errors of Immunity*. 2nd ed. Elsevier; 2020:1229-1239.

Please see the full Prescribing Information.



Education and financial assistance are available through our patient support program, Enzyvant CONNECT


Enzyvant CONNECT is a program that provides you and your child with personalized support as you navigate the congenital athymia journey.

Enzyvant CONNECT is available to all patients with any type of insurance—including commercial plans, Medicare, or Medicaid—as well as patients who are underinsured or have no insurance coverage.

Call **844-ENZCNCT (844-369-2628)** to get connected to personalized support.
We're available Monday–Friday, 8:00 AM to 8:00 PM ET.

Start your enrollment!

 **Sumitomo Pharma** For the latest updates, follow us on [Facebook!](#)

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Dedicated care team

- The Support Liaison will help you understand your child's diagnosis
- The Access Specialist can help you navigate insurance benefits and financial assistance



Access to exclusive resources

- Document organizer
- *Sadie's Search*, a storybook written specifically with your child in mind
- Interactive T-cell progress tracker
- Activity book
- And more!



Co-pay program

- The Enzyvant CONNECT® Commercial Co-Pay Program can help caregivers of eligible commercially insured patients in the US and US territories
- You may receive co-pay assistance for medication-related out-of-pocket costs for RETHYMIC