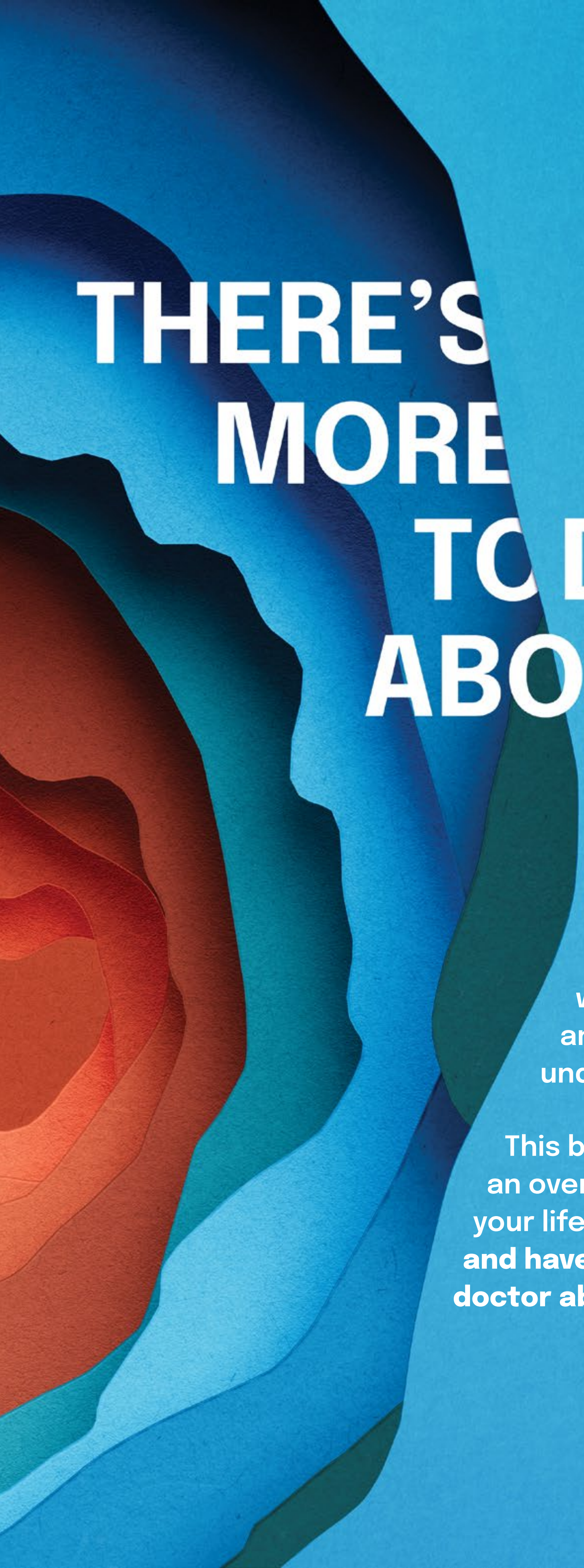
ATTR AMYLOIDOSIS REVEALED™

hATTR
EDUCATIONAL
BROCHURE

EXPLORE ALL THE LAYERS OF hATTR

Take a closer look at hereditary ATTR amyloidosis (hATTR), a genetic and progressive disease.

CECE, living with hATTR



THERE’S MORE TO DISCOVER ABOUT hATTR

hATTR is a hereditary form of ATTR amyloidosis, affecting an estimated 50,000 people worldwide. Since it can impact you and your family, gaining a deeper understanding is essential.

This brochure is intended to give you an overview of hATTR and how it can affect your life. **Use it to deepen your knowledge and have informed conversations with your doctor about your hATTR journey.**

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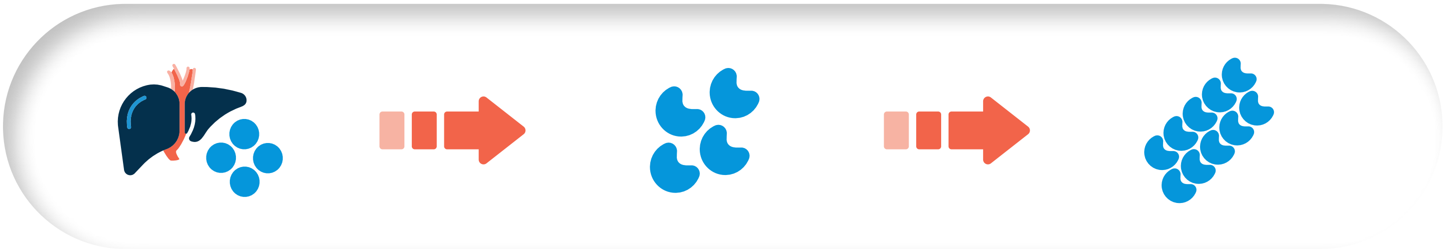
What is hATTR amyloidosis (hATTR)?

hATTR is a rare and underdiagnosed disease caused by the buildup of abnormal proteins called amyloid deposits.

An inherited gene variant, or change, in the transthyretin (TTR) gene causes the TTR protein to misfold and build up as amyloid deposits. The symptoms of hATTR are a result of these amyloid deposits damaging parts of the body, including the **heart, nerves, and digestive system**.

WHAT CAUSES hATTR?



TTR

TTR is a protein made primarily in the liver that carries vitamin A and other substances throughout the body.

Abnormal TTR

In hATTR, a variant, or change, in the TTR gene causes the protein to become toxic to the body by **misfolding** and taking on an **abnormal shape**.

Amyloid deposits

This abnormal shape causes the protein to build up over time in various parts of the body, including the **heart, nerves, and digestive system**. The buildup of abnormal proteins is called **amyloid deposits**.

Who is at risk for hATTR?

Although anyone can be at risk for this disease, it is more common for certain ethnicities, such as people of African, Brazilian, French, Irish, Japanese, Portuguese, or Swedish descent.

There are **more than 120 gene variants** known to be associated with hATTR. The most common variants in the United States are:

	V122I	T60A	V30M
Commonly affected	African Americans (Approximately 1 in 25 may carry the variant)	Irish	Japanese, Portuguese, and Swedish
Age	50s–60s	early 60s	30s–60s
Typical symptoms	Heart- and nerve-related	Heart- and nerve-related	Nerve-related

CAREGIVER CORNER

As a caregiver, you play a critical role in navigating the hATTR journey and its impact on your family. Find more information and resources at ATTRrevealed.com/caregiver

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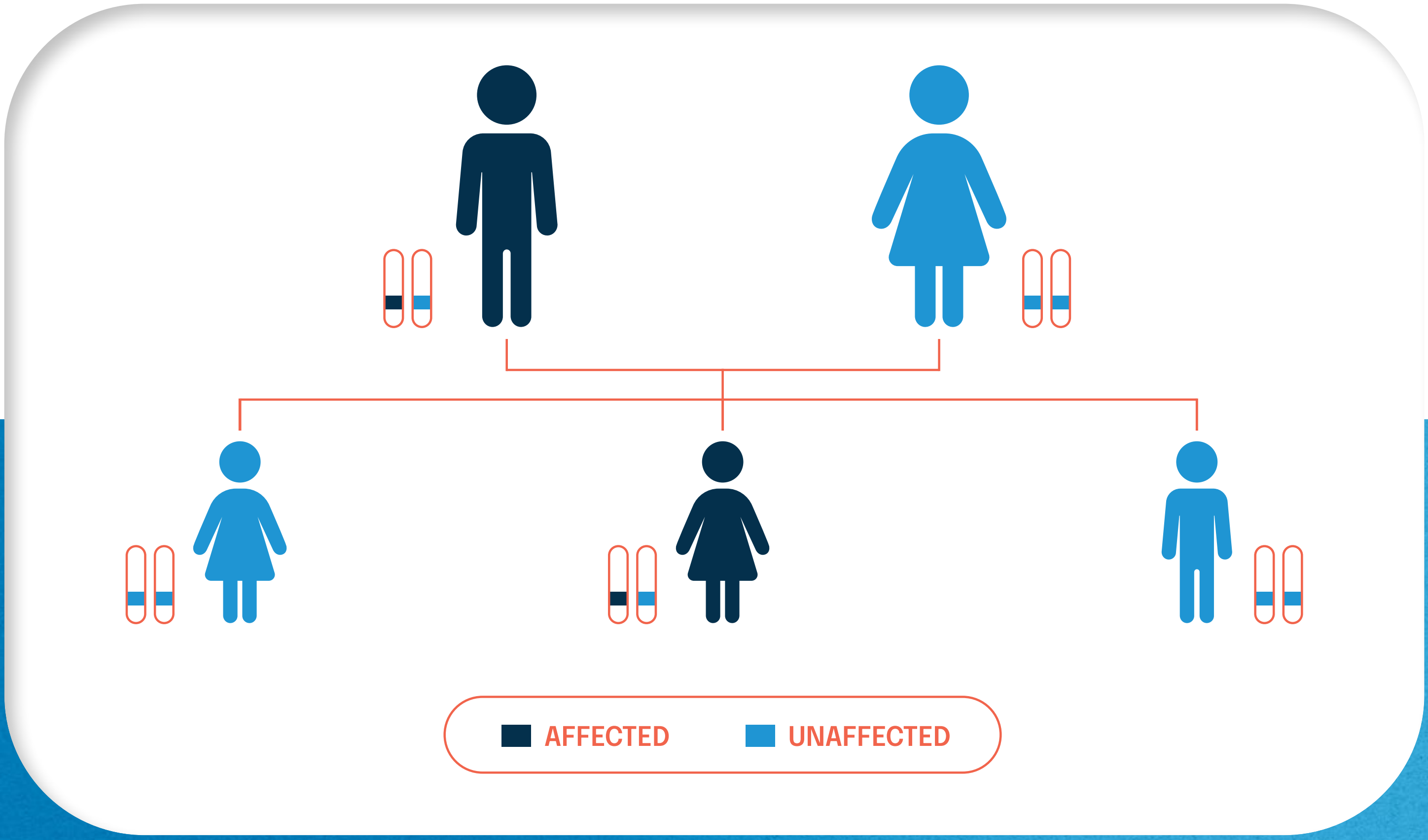
How is hATTR passed down?

If one parent has hATTR, each child has a 50% chance of inheriting the genetic variant that may cause the disease.

A family member may inherit the TTR variant, but having the variant does not necessarily mean that they will develop hATTR.



hATTR can be passed down to children, so it's important to understand how it is inherited in families.

How can hATTR affect your health?

The symptoms of hATTR can vary widely among people with the condition, even within families.

The age that symptoms typically appear ranges from mid-20s to the mid-60s. Because **symptoms of hATTR can worsen over time**, it's important to talk to your doctor about them as soon as possible.

hATTR can affect several parts of your body, including:

The **somatic nervous system**, which is made up of nerves that connect the brain and spinal cord to the skin and muscles, controls sensation, and voluntary movements.

- **Nerve damage** in this system can lead to a range of symptoms, including loss of voluntary movement of the hands and feet, and loss of sensitivity to temperature

The **cardiovascular system**, which is made up of the heart and blood vessels, transports blood through arteries and veins to deliver oxygen to cells and helps to remove metabolic wastes from cells.

- Damage to the heart muscle can lead to **heart failure**

The **autonomic nervous system**, which is made up of nerves that connect the brain and spinal cord to parts of the body, including the heart, stomach, and intestines.

- When this system is not working correctly, it may affect **involuntary bodily functions, such as breathing, digestion, and heart rate**

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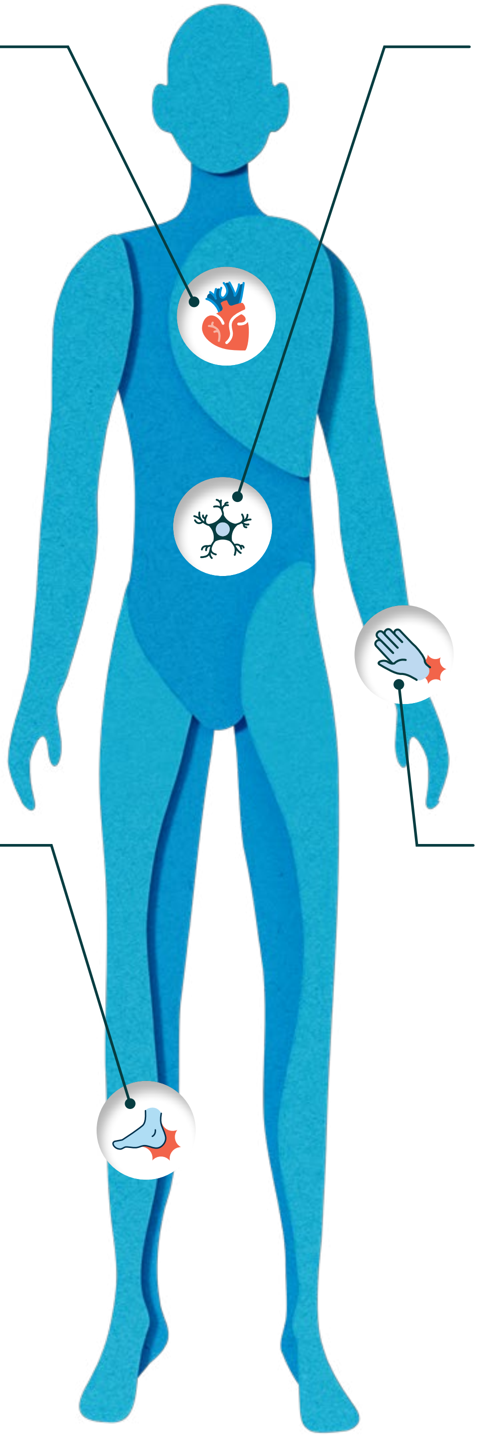
What parts of the body are affected by hATTR?



Symptoms/conditions related to the heart:

- Heart failure
- Abnormal heart rhythms (arrhythmias)
- Irregular heartbeat
- Shortness of breath
- Fatigue
- Fainting
- Leg swelling (edema)

Symptoms related to control over bodily functions:

- Digestive issues (nausea and vomiting, diarrhea, constipation)
- Dizziness upon standing
- Unintentional weight loss
- Recurrent urinary tract infections (UTIs)
- Abnormal sweating
- Sexual dysfunction

Symptoms related to nerves in hands, feet, arms, and legs:

- Tingling
- Numbness
- Burning pain
- Loss of sensitivity to temperature
- Loss of movement control
- Weakness

Symptoms related to the muscles, joints, and tendons:

- Carpal tunnel syndrome
- Lumbar spinal stenosis
- Biceps tendon rupture
- Rotator cuff injury
- Osteoarthritis
- Trigger finger

This is not a complete list of symptoms that may be experienced by people with hATTR. Each person has a different experience, and you may not have all of these symptoms, or you may not have them at the same time.

Why is an accurate diagnosis important?

An accurate diagnosis is essential to ensure your doctor and healthcare team are managing your condition appropriately.

Misdiagnosis or delays in diagnosis are common with hATTR because the symptoms are similar to those of other conditions, which may lead to unnecessary complications.

Have an honest conversation with your doctor

Because hATTR can affect the family, it is important to determine if the cause of your symptoms is genetic. If your doctor thinks you may be experiencing symptoms of hATTR, or if you have a family member living with the disease, your doctor may recommend genetic testing.

Get familiar with the tests

If your doctor thinks you may have hATTR, they may conduct assessments of your heart and nerve function, or order imaging studies or laboratory tests to determine the cause of your symptoms. The diagnostic process may include preliminary and confirmatory tests.

CAREGIVER CORNER

Staying organized is key to getting the most out of doctor's appointments. Consider creating a **Health Record** that includes symptoms, medical history, medications, and contact information for all members of the healthcare team.

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Why consider genetic counseling and testing?

Because hATTR can affect the family, it is important to determine if the cause of your symptoms is genetic.

Your doctor may also recommend that you work with a genetic counselor who can help you and your family learn more about the genetic testing process and if it is right for you.

Genetic testing is needed to:

- Determine whether you have the hereditary form of ATTR. Treatment decisions can vary based on disease type, so it's important to confirm whether you carry a gene variant associated with hATTR amyloidosis
- Indicate whether other family members should get tested to understand their own risk of hATTR

Genetic counselors are trained healthcare professionals who can:

- Work with people who are considering a genetic test and provide guidance after a test
- Help people understand genetics, inheritance, and disease risk
- Discuss the benefits, limitations, and potential implications of genetic testing
- Provide information about support and resources

Explore the diagnosis process with the Guide to Diagnosis at **ATTRrevealed.com/diagnosis**

What is the Alnylam Act® Genetic Testing and Counseling Program?

Alnylam Pharmaceuticals sponsors no-charge, third-party **genetic testing and counseling** for individuals who may carry **one of the 120 or more gene variants** known to be associated with hATTR.

The Alnylam Act Program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes
- Both genetic testing and genetic counseling are available in the US and Canada
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

Learn more at **www.AlnylamAct.com** AlnylamAct

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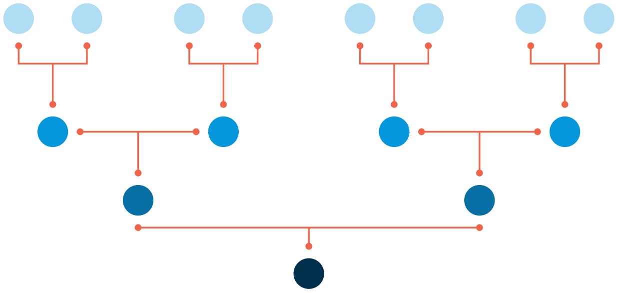
How do you share the news with your family?

Making sure your loved ones are aware of hATTR, that it may run in your family, and the impact it can have on their lives is a crucial step. Here are some tips on discussing hATTR with your family.

PREPARE FOR THE TALK

- **Organize your thoughts.** Create an outline of the topics and points you'd like to talk about during your family conversations
- **Determine how to best have the conversation.** What would be most comfortable for everyone? Some family members may prefer to discuss one-on-one over the phone, or gather in person as a group
- **Come prepared with facts.** Your family will probably have questions and knowing facts about the condition can help your conversation be more productive.

Create a Family Health Tree that maps out your family history of diagnoses, symptoms, and other relevant information. Completing it with loved ones can help educate them about hATTR and how it can be passed down.



Find more information, tools, and resources at www.ATTRrevealed.com

SHARE YOUR hATTR JOURNEY

- **Describe your experience.** Detail the symptoms you first noticed, ways you worked with your doctor to get an accurate diagnosis, and how you manage the condition now
- **Detail that symptoms may vary.** Explain that hATTR can affect several parts of the body, including the nerves, heart, and digestive system. Explain how symptoms may vary widely even among family members
- **Share how misdiagnosis is common.** hATTR has varying symptoms similar to other conditions. Help your family know what to look for, so they can recognize their own symptoms and work with their doctors to get an accurate diagnosis
- **Explain how hATTR affects the entire family.** Help your family understand the hereditary nature of hATTR and their risk. While everyone may not inherit hATTR, your loved ones may be affected by taking on roles as caregivers
- **Encourage working with their doctors.** Urge your family to talk to their doctors about hATTR, genetic counseling and testing. Stress the importance of developing a plan with their care teams for managing hATTR if diagnosed

Speaking with children about hATTR can be difficult, and you may wonder if or when you should have the conversation. If you choose to, be open and encourage questions.

Here are some ways to start the conversation:

- “I feel sad and a little scared myself”
- “What are you thinking right now? It’s okay to be scared, angry, or anything else”
- “I have some news to share with you”
- “We found out what is going on with your dad"

What treatment options are available?

If you are living with hATTR, starting treatment soon after diagnosis is key to managing your symptoms.

There are treatment options available for patients with certain symptoms of hATTR that address the underlying cause of the disease. These work by:

SILENCERS

Reducing the amount of TTR protein made in the body, which can help decrease the formation of amyloid deposits

STABILIZERS

Decreasing the amount of TTR proteins that take on an abnormal shape and form amyloid deposits in the body

If you feel that your current treatment is not meeting your needs, or that your condition is worsening, it's important to **work with your doctor to ensure that you are taking the right steps to manage your disease**.

CAREGIVER CORNER

It's important to speak up during appointments. Being an advocate for your loved one can help the doctor with making decisions on how to manage the disease.

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What other resources are available?

Whether you are starting your hATTR journey or have been managing the disease, there are helpful resources and support for you.

Here are some sources for additional information and assistance:

Amyloidosis Foundation
www.amyloidosis.org

Amyloidosis Research Consortium
www.arci.org

Amyloidosis Support Groups
www.amyloidosissupport.org

Caregiver Action Network
www.caregiveraction.org

The Foundation for Peripheral Neuropathy
www.foundationforpn.org

Global Genes
www.globalgenes.org

Mackenzie's Mission
www.mm713.org

National Alliance for Caregiving
www.caregiving.org

National Organization for Rare Disorders
www.rarediseases.org

oneAMYLOIDOSISvoice
www.oneamyloidosisvoice.com

Go deeper with more tools at **ATTRrevealed.com/resources**

Scan the code or visit www.ATTRrevealed.com to learn more about hATTR and take advantage of other resources.

Alnylam PHARMACEUTICALS

ATTR AMYLOIDOSIS REVEALED™