March 25, 2026

Dear MPS Community,

We value the community's request to remain informed and are committed to sharing timely updates. In response to this, today, we are pleased to share significant news for the Hunter syndrome community. The U.S. Food and Drug Administration has granted Accelerated Approval for AVLAYAH™ (tividenofusp alfa-eknm), for the treatment of neurologic symptoms in pediatric patients weighing at least 5 kg with Hunter syndrome prior to advanced neurologic disease. This approval is based on a reduction of heparan sulfate (HS) in the cerebrospinal fluid (CSF) surrounding the brain and spinal cord. Studies are ongoing to confirm how well it works in improving clinical symptoms. AVLAYAH is not recommended for use in combination with other enzyme replacement therapies for the treatment of Hunter syndrome. This accelerated approval represents the first new FDA-approved treatment for Hunter syndrome in nearly 20 years. Please review our press release for additional details.

This moment reflects years of advocacy leadership, scientific dedication, and the courage and commitment of the children and families who participate in clinical studies. We are deeply grateful to every individual, caregiver, clinician, and advocate who made this possible.

We recognize this approval represents meaningful progress and may offer new possibilities for many families. While this accelerated approval indication does not yet include everyone living with MPS II, we remain committed to continuing our work to address the needs of the broader community.

The ongoing global Phase 2/3 COMPASS study is designed to generate confirmatory evidence and support future regulatory submissions. This study includes adults living with Hunter syndrome and represents an important step toward potentially broadening future access in the United States and globally.

We thank the MPS advocacy community for representing the entire MPS II population and for emphasizing that all individuals living with Hunter syndrome seek innovation and progress. This milestone reflects the strength and persistence of the entire community. We celebrate this progress and remain committed to advancing solutions for everyone living with MPS II.

Families with questions should speak with their healthcare provider. Denali Patient Services is available to support patients, caregivers, and healthcare providers in the United States. For more information, please call 844-DNLI365 (844-365-4365).

This treatment is not currently approved outside the United States. We recognize the urgent need for treatment options worldwide and are working with regulatory authorities to explore different pathways for access in other regions. Families with questions should speak with their healthcare provider.

As we enter this next phase of providing an approved treatment in the United States, we remain committed to working alongside this community, listening closely, and continuing to advance progress together.

Thank you on behalf of the Denali team.

Kim Ramsey
Senior Director, Advocacy

Sydney Gardner
Associate Director, Advocacy

WHAT IS AVLAYAH?

AVLAYAH is approved for the treatment of neurologic symptoms in pediatric patients weighing at least 5 kg with Hunter syndrome prior to advanced neurologic disease. This approval is based on a reduction of heparan sulfate (HS) in the cerebrospinal fluid (CSF) surrounding the brain and spinal cord. Studies are ongoing to confirm how well it works in improving clinical symptoms.

AVLAYAH is not recommended for use in combination with other enzyme replacement therapies for the treatment of Hunter syndrome

IMPORTANT SAFETY INFORMATION

AVLAYAH may cause serious side effects, including hypersensitivity (allergic) reactions such as anaphylaxis which can be life-threatening; infusion-associated reactions (IARs); anemia (low red blood cell count); and Membranous Nephropathy (kidney disorder that affects the filters that help remove wastes and fluids from the kidney). Anaphylaxis can occur early in treatment and after many doses. Seek immediate medical care if symptoms occur.

The most common side effects (in 20% or more of patients) were infusion-associated reactions, upper respiratory infection, ear infection, fever, anemia (low red blood cell count), cough, vomiting, diarrhea, rash, COVID-19, runny or congested nose, falls, headache, skin injuries, and hives.

Contact your healthcare provider right away if you experience any side effects. These are not all the possible side effects of AVLAYAH. You may report side effects to FDA at www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Denali Therapeutics at 1-833-ONE-DNLI (1-833-663-3654).

Please see the full **Prescribing Information** for additional Important Safety Information, including serious side effects.