WHAT IS PRIMARY HYPEROXALURIA?[1-4]

Primary hyperoxaluria is a rare inherited disease caused by a gene change (mutation) that causes calcium oxalate to build up faster than the kidneys can excrete it. This results in recurrent kidney or bladder stones, often occurring at a very young age. Other parts of the body, including the nervous system, heart, retina, and skin, can also be damaged if excess calcium oxalate accumulates. There are three types of primary hyperoxaluria: Type 1, Type 2, and Type 3. Primary hyperoxaluria Type 1 (PH1) is the most common form and accounts for about 80% of all cases.

For more information about primary hyperoxaluria, visit the Oxalosis and Hyperoxaluria Foundation at **https://ohf.org.**

WHAT A POSITIVE GENETIC TEST FOR PRIMARY HYPEROXALURIA TYPE 1 MEANS

PH1 is caused by a mutation in the *AGXT* gene. Genetic testing evaluates whether a person has a mutation in this gene. Testing can give several possible results: a positive result, a negative result, or an uncertain result.

We all have two copies of the *AGXT* gene, one inherited from each parent. When a test result is positive, it means that both copies of the *AGXT* gene have a mutation, and the person has an increased risk to develop symptoms of PH1 during his or her lifetime.

WHAT A POSITIVE GENETIC TEST MEANS FOR YOUR FAMILY

A positive genetic test result may also have important health and social implications for your family members, as PH1 is passed down through families.

Typically, the parents of a person who has PH1 are not affected by the disease. Only one of their two copies of the *AGXT* gene has a mutation. The other copy works normally and is enough to prevent excess buildup of calcium oxalate. If the parents of a person who has PH1 have more children, each child has a 25% risk of being affected with PH1, and a 50% risk that one of their copies of the *AGXT* gene has a mutation.

When a person has a mutation in one of their copies of the *AGXT* gene, other family members may also have the same mutation.

A conversation about PH1 may help you and your family members to plan future pregnancies. It can also help to increase understanding about living with PH1.

GENETIC COUNSELING

Genetic counseling may help you or your family members to better understand the risks, benefits, limitations, and potential implications of genetic testing. Genetic counseling should be performed by a trained health care professional and may be available before, during, or after genetic testing.

In addition to genetic testing, Alnylam is sponsoring no-charge third-party genetic counseling for individuals in the United States who may carry a gene mutation known to be associated with PH1.

To schedule telephone-based genetic counseling, call **1.888.475.3128** and reference the Alnylam Act® program.

Note: Callers will also be asked to provide a doctor's name, address, phone, and fax number, as a detailed summary report will be sent directly to him/her following the genetic counseling session.

AlnylamAct® The Alnylam Act® program was developed to reduce barriers to genetic testing and counseling 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 receives contact information for healthcare professionals who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S. Healthcare professionals who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use or support any Alnylam product.

References: 1. Cochat P, Rumsby G. Primary hyperoxaluria. *N Engl J Med.* 2013;369(7):649-658. **2.** Hopp K, Cogal AG, Bergstralh EJ, et al. Phenotype-Genotype Correlations and Estimated Carrier Frequencies of Primary Hyperoxaluria. *J Am Soc Nephrol.* 2015;26(10):2559-2570. **3.** Hoppe B, Kemper MJ, Bökenkamp A, Portale AA, Cohn RA, Langman CB. Plasma calcium oxalate supersaturation in children with primary hyperoxaluria and end-stage renal failure. *Kidney Int.* 1999;56(1):268-274. **4.** Lorenz, Elizabeth C. et al. "Update on Oxalate Crystal Disease." *Curr rheum rep.* 15.7 (2013): 340.