METHODS OF TREATING FABRY DISEASE IN PATIENTS HAVING A MUTATION IN THE GLA GENE

TECHNICAL FIELD

[0001] Principles and embodiments of the present invention relate generally to the use of pharmacological chaperones for the treatment of Fabry disease, particularly in patients with mutations or variants in the α-galactosidase (GLA) gene.

BACKGROUND

[0002] Many human diseases result from mutations that cause changes in the amino acid sequence of a protein which reduce its stability and may prevent it from folding properly. Proteins generally fold in a specific region of the cell known as the endoplasmic reticulum, or ER. The cell has quality control mechanisms that ensure that proteins are folded into their correct three-dimensional shape before they can move from the ER to the appropriate destination in the cell, a process generally referred to as protein trafficking. Misfolded proteins are often eliminated by the quality control mechanisms after initially being retained in the ER. In certain instances, misfolded proteins can accumulate in the ER before being eliminated. The retention of misfolded proteins in the ER interrupts their proper trafficking, and the resulting reduced biological activity can lead to impaired cellular function and ultimately to disease. In addition, the accumulation of misfolded proteins in the ER may lead to various types of stress on cells, which may also contribute to cellular dysfunction and disease.

[0003] Such mutations can lead to lysosomal storage disorders (LSDs), which are characterized by deficiencies of lysosomal enzymes due to mutations in the genes encoding the lysosomal enzymes. The resultant disease causes the pathologic accumulation of substrates of those enzymes, which include lipids, carbohydrates, and polysaccharides. Although there are many different mutant genotypes associated with each LSD, many of the mutations are missense mutations which can lead to the production of a less stable enzyme. These less stable enzymes are sometimes prematurely degraded by the ER-associated degradation pathway. This results in the enzyme deficiency in the lysosome, and the pathologic accumulation of substrate. Such mutant enzymes are sometimes referred to in the pertinent art as "folding mutants" or "conformational mutants."

[0004] Fabry Disease is a LSD caused by a mutation to the GLA gene, which encodes the enzyme α-galactosidase A (α-Gal A). α-Gal A is required for glycosphingolipid metabolism. The mutation causes the substrate globotriaosylceramide (GL-3) to accumulate in various tissues and organs. Males with Fabry disease are hemizygotes because the disease genes are encoded on the X chromosome. Fabry disease is estimated to affect 1 in 40,000 and 60,000 males, and occurs less frequently in females.

[0005] There have been several approaches to treatment of Fabry disease. One approved therapy for treating Fabry disease is enzyme replacement therapy (ERT), which typically involves intravenous, infusion of a purified form of the corresponding wild-type protein. Two α-Gal A products are currently available for the treatment of Fabry disease: agalsidase alfa (Replagal®, Shire Human Genetic Therapies) and agalsidase beta (Fabrazyme®; Sanofi Genzyme Corporation). ERT has several drawbacks, however. One of the main complications with ERT is rapid degradation of the infused protein, which leads to the need for numerous costly high dose infusions. ERT has several additional caveats, such as difficulties with large-scale generation, purification, and storage of properly folded protein; obtaining glycosylated native protein; generation of an anti-protein immune response; and inability of protein to cross the blood-brain barrier to mitigate central nervous system pathologies (i.e., low bioavailability). In addition, replacement enzyme cannot penetrate the heart or kidney in sufficient amounts to reduce substrate accumulation in the renal podocytes or cardiac myocytes, which figure prominently in Fabry pathology.

[0006] Another approach to treating some enzyme deficiencies involves the use of small molecule inhibitors to reduce production of the natural substrate of deficient enzyme proteins, thereby ameliorating the pathology. This "substrate reduction" approach has been specifically described for a class of about 40 LSDs that include glycosphingolipid storage disorders. The small molecule inhibitors proposed for use as therapy are specific for inhibiting the enzymes involved in synthesis of glycolipids, reducing the amount of cellular glycolipid that needs to be broken down by the deficient enzyme.

[0007] A third approach to treating Fabry disease has been treatment with what are called pharmacological chaperones (PCs). Such PCs include small molecule inhibitors of α-Gal A, which can bind to the α-Gal A to increase the stability of both mutant enzyme and the corresponding wild type. However, patients for PC therapy should have an amenable mutation

or variant which results in the production of an enzyme that has the potential to be stabilized and folded into a conformation that permits trafficking out of the ER.

[0008] Thus, even when Fabry disease is diagnosed by detecting deficient α-Gal A activity in plasma or peripheral leukocytes (WBCs), it is very difficult, if not impossible, to predict whether a particular Fabry patient will respond to treatment with a PC. Thus, there remains a need to identify new GLA mutations or variants that will be responsive to a PC and make available new methods of treatment to Fabry patients with these mutations or variants.

SUMMARY

[0009] One aspect of the invention pertains to a method of treating a patient diagnosed with Fabry disease. The method comprises administering to the patient a therapeutically effective dose of a pharmacological chaperone for α-Gal A, wherein the patient has a missense mutation of the nucleic acid sequence encoding α-Gal A. In one or more embodiments, the mutation is N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T,

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Q416H, Q416L, L417I, E418A, E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, M423L, M423T, S424L, L425F, D427N, or L429R. In various embodiments, these mutations are relative to SEQ ID NO: 2. An additional aspect of the invention pertains to a medicament for treating a patient diagnosed with Fabry disease who has a missense mutation of the nucleic acid sequence encoding α-Gal A. In one or more embodiments, the mutation is provided above. In various embodiments, these mutations are relative to SEQ ID NO: 2.

[0010] In some embodiments, the pharmacological chaperone or medicament comprises migalastat or salt thereof. In one or more embodiments, the dose of migalastat or salt thereof is from about 100 mg to about 150 mg free base equivalent (FBE). In some embodiments, the salt of migalastat is migalastat hydrochloride. In one or more embodiments, the dose is about 150 mg every other day of migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt. In some embodiments, the migalastat or salt thereof is administered orally or by injection. These embodiments may be combined with one another or with other embodiments of the invention, for example embodiments relating to a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease, use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease as well as embodiments relating to amenable mutations, suitable PCs and dosages, formulations and routes of administration thereof.

[0011] Another aspect of the invention pertains to a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease. The method comprises administering to a patient a therapeutically effective dose of a pharmacological chaperone for α-Gal A, wherein the patient has a missense mutation in the nucleic acid sequence encoding α-Gal A. Accordingly, an additional aspect of the invention pertains to a medicament for enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease who has a missense mutation of the nucleic acid sequence encoding α-Gal A. In one or more embodiments, the mutation is provided below.

[0012] In one or more embodiments, the mutation is N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F,

L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, H125D, H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, D136N, D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, G144A, G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, Y151D, Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, F159V, F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, F169L, F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, E178A, E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, H186D, H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D,

A190G, A190S, A190T, A190V, L191M, L191V, N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, S197I, S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, L206V, Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, N215H, N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, I219M, I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, F229Y, A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, K240M, K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, T246R, S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, E251V, R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, P259A, P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, L275I, W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, L286V, A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, N298T, D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, K308Q, K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, D315Y, V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, G325V, K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E, Q330H, Q330K, L331H, L331P, L331R, L331V, R332G, R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, F337L, F337V, F337Y, E338A, E338D, E338G, V339M, E341A,

E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, W349C, W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, I359F, I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, T366P, T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, G373C, K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, P380R, P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, L388R, L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N, K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, F396L, F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, R402M, R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, N408T, P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, E418A, E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, M423L, M423T, S424L, L425F, D427N, or L429R. In various embodiments, these mutations are relative to SEQ ID NO: 2.

[0013] In some embodiments, the pharmacological chaperone comprises migalastat or salt thereof. In one or more embodiments, the dose of migalastat or salt thereof is from about 100 mg to about 150 mg FBE. In some embodiments, the salt of migalastat is migalastat hydrochloride. In one or more embodiments, the dose is about 150 mg every other day of migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt. In some embodiments, the migalastat or salt thereof is administered orally or by injection. These embodiments may be combined with one another or with other embodiments of the invention, for example embodiments relating to a method of treating a patient with Fabry disease, use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry

disease as well as embodiments relating to amenable mutations, suitable PCs and dosages, formulations and routes of administration thereof.

[0014] Another aspect of the invention pertains to use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease, wherein the patient has a missense mutation in the nucleic acid sequence encoding α-Gal A. In one or more embodiments, the mutation is N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, H125D, H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, D136N, D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, G144A, G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, Y151D, Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V,

D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, F159V, F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, F169L, F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, E178A, E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, H186D, H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, L191V, N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, S197I, S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, L206V, Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, N215H, N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, I219M, I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, F229Y, A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, K240M, K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, T246R, S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, E251V, R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, P259A, P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, L275I, W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, L286V, A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, N298T, D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, K308Q, K308R,

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[0015] In some embodiments, the pharmacological chaperone comprises migalastat or salt thereof. In one or more embodiments, the dose of migalastat or salt thereof is from about 100 mg to about 150 mg FBE. In some embodiments, the salt of migalastat is migalastat

hydrochloride. In one or more embodiments, the dose is about 150 mg every other day of migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt. In some embodiments, the migalastat or salt thereof is administered orally or by injection. These embodiments may be combined with one another or with other embodiments of the invention, for example embodiments relating to a method of treating a patient with Fabry disease, a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease, or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease as well as embodiments relating to amenable mutations, suitable PCs and dosages, formulations and routes of administration thereof.

[0016] Another aspect of the invention pertains to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease, wherein the patient has a missense mutation in the nucleic acid sequence encoding α-Gal A. In one or more embodiments, the mutation is N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T,

A121V, Y123D, Y123F, Y123N, Y123S, V124I, H125D, H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, D136N, D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, G144A, G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, Y151D, Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, F159V, F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, F169L, F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, E178A, E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, H186D, H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, L191V, N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, S197I, S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, L206V, Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, N215H, N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, I219M, I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, F229Y, A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, K240M, K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, T246R, S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, E251V, R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, P259A, P259T, G260W, G261A, N263H, N263T,

D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, L275I, W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, L286V, A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, N298T, D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, K308Q, K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, D315Y, V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, G325V, K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E, Q330H, Q330K, L331H, L331P, L331R, L331V, R332G, R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, F337L, F337V, F337Y, E338A, E338D, E338G, V339M, E341A, E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, W349C, W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, I359F, I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, T366P, T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, G373C, K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, P380R, P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, L388R, L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N, K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, F396L, F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, R402M, R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, N408T, P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, E418A, E418D,

E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, M423L, M423T, S424L, L425F, D427N, or L429R. In various embodiments, these mutations are relative to SEQ ID NO: 2.

[0017] In some embodiments, the pharmacological chaperone comprises migalastat or salt thereof. In one or more embodiments, the dose of migalastat or salt thereof is from about 100 mg to about 150 mg FBE. In some embodiments, the salt of migalastat is migalastat hydrochloride. In one or more embodiments, the dose is about 150 mg every other day of migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt. In some embodiments, the migalastat or salt thereof is administered orally or by injection. These embodiments may be combined with one another or with other embodiments of the invention, for example embodiments relating to a method of treating a patient with Fabry disease, a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease or use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease as well as embodiments relating to amenable mutations, suitable PCs and dosages, formulations and routs of administration thereof.

[0018] Another aspect of the invention pertains to migalastat or a salt thereof for use in a method for treatment of Fabry disease in a human patient in, wherein the patient has an α-galactosidase A mutation selected from the group consisting of those mutations provided in Table 2.

[0019] Another aspect of the invention pertains to a method of treating a patient diagnosed with Fabry disease, wherein the patient has a HEK assay amenable mutation in α-galactosidase A disclosed in a pharmacological reference table as disclosed herein. This aspect can have any of the features described in the other aspects as disclosed herein.

[0020] Another aspect of the invention pertains to a method of enhancing α-galactosidase A in a patient diagnosed with or suspected of having Fabry disease, wherein the patient has a HEK assay amenable mutation in α-galactosidase A disclosed in a pharmacological reference table as disclosed herein. This aspect can have any of the features described in the other aspects as disclosed herein.

[0021] Some embodiments relate to a method of treating Fabry disease in a subject. Mutation information corresponding to the subject is accessed. The mutation information identifies one or more α-galactosidase A mutations. Based on the mutation information, it is

determined that the subject has at least one mutation as identified in Table 2 and/or at least one mutation of: N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, H125D, H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, D136N, D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, G144A, G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, Y151D, Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, F159V, F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, F169L, F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S,

L177V, L177W, E178A, E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, H186D, H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, L191V, N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, S197I, S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, L206V, Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, N215H, N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, I219M, I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, F229Y, A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, K240M, K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, T246R, S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, E251V, R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, P259A, P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, L275I, W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, L286V, A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, N298T, D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, K308Q, K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, D315Y, V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, G325V, K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E,

Q330H, Q330K, L331H, L331P, L331R, L331V, R332G, R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, F337L, F337V, F337Y, E338A, E338D, E338G, V339M, E341A, E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, W349C, W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, I359F, I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, T366P, T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, G373C, K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, P380R, P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, L388R, L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N, K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, F396L, F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, R402M, R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, N408T, P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, E418A, E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, M423L, M423T, S424L, L425F, D427N, or L429R. In response to the determination, migalastat or a salt thereof is administered to the subject.

[0022] The at least one mutation can include one or more mutations of α-galactosidase A at amino acid residues 5-14, 17-18, 20-30, 32-33, 36-39, 41, 43, 45-46, 48, 50-51, 53-56, 58-62, 64-89, 91, 96-99, 101-102, 104-110, 113-117, 121, 123-131, 133, 135-141, 143-153, 156-162, 164-167, 169, 171, 173, 175-178, 180-182, 184-201, 203, 204, 206-222, 224, 227- 230, 232-233, 235, 237-261, 263-265, 267-270, 272-273, 275, 277-278, 280-286, 288-289, 291-292, 294-295, 297-300, 302-304, 306-322, 324-327, 329-339, 341, 343-344, 346-357, 359, 362-371, 373- 377, 379-381, 383-388, 391-425, 427, or 429, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2

[0023] Determining that the subject has at least one mutation as identified in Table 2 can include initiating a query of a data store that identifies two or more mutations from a set of mutations identified in Table 2 and receiving a query result that identifies the at least one mutation is represented in the mutation information and also in Table 2. The data store may further identify two or more mutations from another set of mutations (e.g., identified in Table 2). The data store may identify at least 10%, 25%, 50%, 75%, 90% or 95% of the mutations as included in Table 1 and/or at least 10%, 25%, 50%, 75%, 90% or 95% of the mutations as included in Table 2. The query may be initiated by accessing a particular webpage hosted by a web server that controls a data store identifying at least some of the mutations in Table 2. The query may be initiated by accessing a particular webpage on a website; providing input at the particular webpage that identifies at least part of the mutation information; and selecting an option at the webpage to submit, to a web server, an electronic request to perform the query, the electronic request including a representation of the input. The query result may be received from the web server in response to the query and may be displayed at the particular webpage or another webpage on the website.

[0024] The migalastat or salt thereof may be administered to the subject every other day. Administering the migalastat or salt thereof can include administering the migalastat or salt thereof in a dose of about 100 to about 150 mg free base equivalent of the migalastat of salt thereof; or administering about 123 mg free base equivalent of the migalastat of salt thereof. The migalastat or salt thereof may enhance α-galactosidase A activity in the subject. The at least one mutation can include an HEK assay amenable mutation in α-galactosidase A. The migalastat or salt thereof may be administered orally or by injection.

[0025] In some embodiments, a computer-implemented method is provided. An electronic communication is received. The electronic communication corresponds to an identification of a particular mutation. A data store is queried using the identification of the particular mutation. The data store includes an identification of each of a set of amenable mutations. Each of the set of amenable mutations corresponds to a mutation listed in Table 2. A result of the query is detected, the result being indicative of whether the particular mutation is represented in the set of amenable mutations. Based on the response, an output is generated that is indicative of a suitability of treating a patient with the particular mutation with migalastat or a migalastat salt. The output.is transmitted.

[0026] The electronic communication can include the identification of the particular mutation in a first format, and the method can further include determining that the first format differs from a second format used by the data store; extracting one or more components from the identification; generating a second identification based on the components, the second identification being in the second format; transmitting the second identification; and receiving a second electronic communication that indicates that the second identification corresponds to the first identification. The data store may be queried in response to receiving the second electronic communication. The data store may further include an identification of another set of amenable mutations. Each of the second set of amenable mutations corresponds to a mutation listed in Table 1, and the result may be further indicative of whether the particular mutation is represented in the second set of amenable mutations. The result may include a binary indication as to whether migalastat or migalastat salt is a suitable treatment for a condition attributed to the particular mutation. The identification of the particular mutation may correspond to input detected at a webpage (generated at least in part based on webpage data transmitted to a user device from which the electronic device is received). The data store may identify at least 10%, at least 25%, at least 50%, at least 75% or at least 90% of the mutations listed in Table 2.

[0027] In some embodiments, a computer-implemented method is provided. A data set unit storing a data set is accessed that identifies, for each mutation of a set of mutations, a degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the mutation is present. The set of mutations includes one or more mutations listed in Table 2. A communication is received that identifies one or more particular mutations. The data set unit is queried using a representation of the one or more particular mutations. A result of the query is detected. The result indicates, for each particular mutation of the one or more particular mutations, the degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the particular mutation is present. A metric is determined that corresponds to a predicted efficacy of treating a patient having the one or more particular mutations with migalastat or a migalastat salt. The metric is output.

[0028] The one or more particular mutations may include a plurality of particular mutations, and determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations. The metric can be a binary indication as to whether a

condition associated with the one or more particular mutations are amenable to treatment with migalastat or a migalastat salt. the metric may include a number, category or descriptor indicating a predicted extent to which a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt. The result of the query may indicate, for a particular mutation of the one or more particular mutations and as a result of the particular mutation not being detected within the data set, that the α-Gal A activity corresponding to the particular mutation is not responsive to migalastat or a migalastat salt. The set of mutations may further include one or more mutations listed in Table 1. The one or more particular mutations may include a plurality of particular mutations, and determining the metric may include identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

[0029] In some instances, a method of treating Fabry disease in a subject is provided. Mutation information is accessed that corresponds to the subject. The mutation information identifies one or more α-galactosidase A mutations. It is determined, based on the mutation information, that the subject has a mutation for which □-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 □M migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α -Gal A corresponding to the mutation. In response to the determination, migalastat or a salt thereof is administered to the subject.

[0030] The α-Gal A activity may be defined as the nmoles of free 4-MU released per milligram of protein per hour. The determination can include determining that the subject has a mutation for which α-Gal A activity is at least 1%, at least 5%, at least 10%, at least 25%, at least 50% or at least 100% greater than the reference α-Gal A activity. The determination can include querying a data store with an identification of the one or more α-galactosidase A mutations and receiving a result of the query. The result can indicate that representation of the mutation is included in the data store. The result can include one or more values associated with a representation of the mutation in the data store, and the method can further include comparing the one or more values or a processed version thereof to a predefined threshold.

[0031] In some instances, a method is provided. Mutation information corresponding to a subject is access. The mutation information identifies one or more α-galactosidase A mutations. It is determined, based on the mutation information, that the subject has a mutation for which α-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 μM migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α -Gal A corresponding to the mutation. In response to the determination, an indication is output that the mutation is amenable to treatment with migalastat or a salt thereof.

[0032] The α-Gal A activity can be defined as the nmoles of free 4-MU released per milligram of protein per hour. The determination can include determining that the subject has a mutation for which α-Gal A activity is at least 1%, at least 5%, at least 10%, at least 25%, at least 50% or at least 100% greater than the reference α-Gal A activity. The determination can include querying a data store with an identification of the one or more α-galactosidase A mutations and receiving a result of the query. The result can indicate that representation of the mutation is included in the data store. The result can include one or more values associated with a representation of the mutation in the data store, and the method can further include comparing the one or more values or a processed version thereof to a predefined threshold. The method can include receiving, from a user device, a first communication that includes the mutation information, and outputting the indication can include, transmitting a second communication to the user device, the second communication including the indication.

[0033] In some instances, a system is provided. The system includes one or more data processors and a non-transitory computer readable storage medium containing instructions which, when executed on the one or more data processors, cause the one or more data processors to perform part or all of one or more methods disclosed herein. In some instances, computer-program product is provided that is tangibly embodied in a non-transitory machine-readable storage medium. The computer-program product can include instructions configured to cause one or more data processors to perform part or all of one or more methods disclosed herein.

[0034] Another aspect of the invention pertains to a method for diagnosing in a subject Fabry disease which is amenable to treatment with migalastat or a salt thereof, the method

comprising determining whether α-Gal A in a sample from the subject has an amino acid sequence comprising at least one mutation as identified in Table 2; wherein if the α-Gal A in the sample from the subject has an amino acid sequence comprising such a mutation, the subject has, or is at risk of developing, Fabry disease which is amenable to treatment with migalastat or a salt thereof. In one or more embodiments, the subject has one or more symptoms of Fabry disease. In other embodiments, the subject does not have any symptoms of Fabry disease. In one or more embodiments, the subject is an infant. In one or more embodiments, the subject is a male. In one or more embodiments, the subject is a female. In one or more embodiments, the subject has a family history of Fabry disease. In one or more embodiments, the subject is the daughter of a classically affect male Fabry patient.

[0035] Another aspect of the invention pertains to a method for identifying a subject with Fabry disease which is amenable to treatment with migalastat or a salt thereof, the method comprising determining whether α-Gal A in a sample from the subject has an amino acid sequence comprising at least one mutation as identified in Table 2; wherein if the α-Gal A in the sample from the subject has an amino acid sequence comprising such a mutation, the subject has, or is at risk of developing, Fabry disease which is amenable to treatment with migalastat or a salt thereof. In one or more embodiments, the subject has one or more symptoms of Fabry disease. In other embodiments, the subject does not have any symptoms of Fabry disease. In one or more embodiments, the subject is an infant. In one or more embodiments, the subject is a male. In one or more embodiments, the subject is a female. In one or more embodiments, the subject has a family history of Fabry disease. In one or more embodiments, the subject is the daughter of a classically affect male Fabry patient.

[0036] Another aspect of the invention pertains to a method for diagnosing in a subject Fabry disease which is amenable to treatment with migalastat or a salt thereof, the method comprising determining whether the GLA gene in a sample from a subject comprises a point mutation compared to the nucleic acid sequence of SEQ ID NO: 1; if the GLA gene in the sample comprises such a point mutation, determining whether the point mutation results in an amino acid mutation of α-Gal A as identified in Table 2; wherein the point mutation results in an amino acid mutation of α-Gal A as identified in Table 2, the subject has, or is at risk of developing, Fabry disease which is amenable to treatment with migalastat or a salt thereof. In other embodiments, the subject does not have any symptoms of Fabry disease. In one or more embodiments, the subject is an embryo. In one or more embodiments, the subject is an infant.

In one or more embodiments, the subject is a male. In one or more embodiments, the subject is a female. In one or more embodiments, the subject has a family history of Fabry disease. In one or more embodiments, the subject is the daughter of a classically affect male Fabry patient.

[0037] Another aspect of the invention pertains to a method for identifying a subject with Fabry disease which is amenable to treatment with migalastat or a salt thereof, the method comprising determining whether the GLA gene in a sample from a subject comprises a point mutation compared to the nucleic acid sequence of SEQ ID NO: 1; if the GLA gene in the sample comprises such a point mutation, determining whether the point mutation results in an amino acid mutation of α-Gal A as identified in Table 2; wherein the point mutation results in an amino acid mutation of α-Gal A as identified in Table 2, the subject has, or is at risk of developing, Fabry disease which is amenable to treatment with migalastat or a salt thereof. In other embodiments, the subject does not have any symptoms of Fabry disease. In one or more embodiments, the subject is an embryo. In one or more embodiments, the subject is an infant. In one or more embodiments, the subject is a male. In one or more embodiments, the subject is a female. In one or more embodiments, the subject has a family history of Fabry disease. In one or more embodiments, the subject is the daughter of a classically affect male Fabry patient.

[0038] Various embodiments are listed below. It will be understood that the embodiments listed below may be combined not only as listed below, but in other suitable combinations in accordance with the scope of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0039] FIGS. 1A-E shows the full DNA sequence of human wild type GLA gene (SEQ ID NO: 1);

[0040] FIG. 2 shows the wild-type α-Gal A protein (SEQ ID NO: 2); and

[0041] FIG. 3 shows the nucleic acid sequence encoding the wild-type α-Gal A protein (SEQ ID NO: 3).

[0042] FIG. 4A shows an exemplary interaction system to generate treatment classifications based on mutation data.

[0043] FIG. 4B shows a schematic view of an exemplary mutation classifier system.

[0044] FIG. 5 illustrates an exemplary process for using mutation data to generate predictive metrics.

[0045] FIG. 6 illustrates an exemplary process for using mutation data to generate predictive outputs.

[0046] FIG. 7 illustrates exemplary mutation representations for to be used to facilitate assessments of mutation-based effects.

[0047] FIG. 8 illustrates an exemplary interface to facilitate mutation-based treatment classifications.

DETAILED DESCRIPTION

[0048] Before describing several exemplary embodiments of the invention, it is to be understood that the invention is not limited to the details of construction or process steps set forth in the following description. The invention is capable of other embodiments and of being practiced or being carried out in various ways.

[0049] As described above, it is very difficult, if not impossible, to predict whether a particular Fabry patient will respond to treatment with a PC. Currently, when a patient is assessed, it is necessary first to determine the particular mutation in α-Gal A, then to test the patient's specific mutated form of α-Gal A in an assay to determine whether or not the mutation is amenable to treatment with migalastat. The migalastat amenability testing is typically performed by someone other than the clinician that is assessing the patient for treatment. This testing takes time and delays the start of treatment.

[0050] Accordingly, various aspects of the invention pertain to identification of new GLA mutations in Fabry patients who will respond to treatment with pharmacological chaperones. Other aspects of the invention pertain to the treatment of these Fabry patients, as well. For example, it has been unexpectedly discovered that the low α-Gal A activity resulting from the missense mutations in α-Gal A shown in Table 2 can be increased when exposed to pharmacological chaperones, even though no patients have previously been identified with these particular mutations. By extension, patients with these mutations are expected to be responsive to treatment with pharmacological chaperones.

[0051] Use of the information in Table 2 prevents the delay of starting treatment, as further testing of the PC amenability of the patient's α-Gal A is no longer necessary. Instead, after determining the patient's particular mutation, the clinician can consult a list of α-Gal A mutations (e.g. including one or more mutations listed in Table 2) and, if the patient's mutation is in the list, can begin treatment immediately.

[0052] The identification of these new mutations can also be used to determine whether a subject, including an embryo or a neonatal infant, is at risk of developing Fabry disease before the appearance of symptoms. In one or more embodiments, the subject can be at risk for developing Fabry disease, such as having a family history of Fabry disease.

[0053] Definitions

[0054] The terms used in this specification generally have their ordinary meanings in the art, within the context of this invention and in the specific context where each term is used. Certain terms are discussed below, or elsewhere in the specification, to provide additional guidance to the practitioner in describing the compositions and methods of the invention and how to make and use them.

[0055] The term "Fabry disease" refers to an X-linked inborn error of glycosphingolipid catabolism due to deficient lysosomal α-Gal A activity. This defect causes accumulation of the substrate globotriaosylceramide (("GL-3", also known as Gb_3 or ceramide trihexoside) and related glycosphingolipids in vascular endothelial lysosomes of the heart, kidneys, skin, and other tissues. Another substrate of the enzyme is plasma globotriaosylsphingosine ("plasma lyso-Gb_3").

[0056] A "carrier" is a female who has one X chromosome with a defective α-Gal A gene and one X chromosome with the normal gene and in whom X chromosome inactivation of the normal allele is present in one or more cell types. A carrier is often diagnosed with Fabry disease.

[0057] A "patient" refers to a subject who has been diagnosed with or is suspected of having a particular disease. The patient may be human or animal.

[0058] A "Fabry patient" refers to an individual who has been diagnosed with or suspected of having Fabry disease and has a mutated α-Gal A as defined further below. Characteristic markers of Fabry disease can occur in male hemizygotes and female carriers with the same prevalence, although females typically are less severely affected.

[0059] Human α-galactosidase A (α-Gal A) refers to an enzyme encoded by the human GLA gene. The full DNA sequence of α-Gal A, including introns and exons, is available in GenBank Accession No. X14448.1 and shown in FIGS. 1A-E (SEQ ID NO: 1). The human α-Gal A enzyme consists of 429 amino acids and is available in GenBank Accession Nos. X14448.1 and U78027 and shown in FIG. 2 (SEQ ID NO: 2). The nucleic acid sequence that

only includes the coding regions (i.e. exons) of SEQ ID NO: 1 is shown in FIG. 3 (SEQ ID NO: 3).

[0060] The term "mutant protein" includes a protein which has a mutation in the gene encoding the protein which results in the inability of the protein to achieve a stable conformation under the conditions normally present in the ER. The failure to achieve a stable conformation results in a substantial amount of the enzyme being degraded, rather than being transported to the lysosome. Such a mutation is sometimes called a "conformational mutant." Such mutations include, but are not limited to, missense mutations, and in-frame small deletions and insertions.

[0061] As used herein in one embodiment, the term "mutant α-Gal A" includes an α-Gal A which has a mutation in the gene encoding α-Gal A which results in the inability of the enzyme to achieve a stable conformation under the conditions normally present in the ER. The failure to achieve a stable conformation results in a substantial amount of the enzyme being degraded, rather than being transported to the lysosome.

[0062] As used herein, the term "specific pharmacological chaperone" ("SPC") or "pharmacological chaperone" ("PC") refers to any molecule including a small molecule, protein, peptide, nucleic acid, carbohydrate, etc. that specifically binds to a protein and has one or more of the following effects: (i) enhances the formation of a stable molecular conformation of the protein; (ii) induces trafficking of the protein from the ER to another cellular location, preferably a native cellular location, i.e., prevents ER-associated degradation of the protein; (iii) prevents aggregation of misfolded proteins; and/or (iv) restores or enhances at least partial wild-type function and/or activity to the protein. A compound that specifically binds to e.g., α-Gal A, means that it binds to and exerts a chaperone effect on the enzyme and not a generic group of related or unrelated enzymes. More specifically, this term does not refer to endogenous chaperones, such as BiP, or to non-specific agents which have demonstrated non-specific chaperone activity against various proteins, such as glycerol, DMSO or deuterated water, i.e., chemical chaperones. In one or more embodiments of the present invention, the PC may be a reversible competitive inhibitor. In one embodiment, the PC is migalastat or a salt thereof. In another embodiment, the PC is migalastat free base (e.g., 123 mg of migalastat free base). In yet another embodiment, the PC is a salt of migalastat (e.g., 150 mg of migalastat HCl).

[0063] A "competitive inhibitor" of an enzyme can refer to a compound which structurally resembles the chemical structure and molecular geometry of the enzyme substrate to bind the enzyme in approximately the same location as the substrate. Thus, the inhibitor competes for the same active site as the substrate molecule, thus increasing the Km. Competitive inhibition is usually reversible if sufficient substrate molecules are available to displace the inhibitor, i.e., competitive inhibitors can bind reversibly. Therefore, the amount of enzyme inhibition depends upon the inhibitor concentration, substrate concentration, and the relative affinities of the inhibitor and substrate for the active site.

[0064] As used herein, the term "specifically binds" refers to the interaction of a pharmacological chaperone with a protein such as α-Gal A, specifically, an interaction with amino acid residues of the protein that directly participate in contacting the pharmacological chaperone. A pharmacological chaperone specifically binds a target protein, e.g., α-Gal A, to exert a chaperone effect on the protein and not a generic group of related or unrelated proteins. The amino acid residues of a protein that interact with any given pharmacological chaperone may or may not be within the protein's "active site." Specific binding can be evaluated through routine binding assays or through structural studies, e.g., co-crystallization, NMR, and the like. The active site for α-Gal A is the substrate binding site.

[0065] "Deficient α-Gal A activity" refers to α-Gal A activity in cells from a patient which is below the normal range as compared (using the same methods) to the activity in normal individuals not having or suspected of having Fabry or any other disease (especially a blood disease).

[0066] As used herein, the terms "enhance α-Gal A activity" or "increase α-Gal A activity" refer to increasing the amount of α-Gal A that adopts a stable conformation in a cell contacted with a pharmacological chaperone specific for the α-Gal A, relative to the amount in a cell (preferably of the same cell-type or the same cell, e.g., at an earlier time) not contacted with the pharmacological chaperone specific for the α-Gal A. This term also refers to increasing the trafficking of α-Gal A to the lysosome in a cell contacted with a pharmacological chaperone specific for the α-Gal A, relative to the trafficking of α-Gal A not contacted with the pharmacological chaperone specific for the protein. These terms refer to both wild-type and mutant α-Gal A. In one embodiment, the increase in the amount of α-Gal A in the cell is measured by measuring the hydrolysis of an artificial substrate in lysates from

cells that have been treated with the PC. An increase in hydrolysis is indicative of increased α-Gal A activity.

[0067] The term "α-Gal A activity" refers to the normal physiological function of a wild-type α-Gal A in a cell. For example, α-Gal A activity includes hydrolysis of GL-3.

[0068] A "responder" is an individual diagnosed with or suspected of having a lysosomal storage disorder, such, for example Fabry disease, whose cells exhibit sufficiently increased α-Gal A activity, respectively, and/or amelioration of symptoms or enhancement in surrogate markers, in response to contact with a PC. Non-limiting examples of enhancements in surrogate markers for Fabry are lyso-GB3 and those disclosed in US Patent Application Publication No. US 2010-0113517, which is hereby incorporated by reference in its entirety.

[0069] Non-limiting examples of improvements in surrogate markers for Fabry disease disclosed in US 2010/0113517 include increases in α-Gal A levels or activity in cells (e.g., fibroblasts) and tissue; reductions in of GL-3 accumulation; decreased plasma concentrations of homocysteine and vascular cell adhesion molecule-1 (VCAM-1); decreased GL-3 accumulation within myocardial cells and valvular fibrocytes; reduction in plasma lyso-Gb3; reduction in cardiac hypertrophy (especially of the left ventricle), amelioration of valvular insufficiency, and arrhythmias; amelioration of proteinuria; decreased urinary concentrations of lipids such as CTH, lactosylceramide, ceramide, and increased urinary concentrations of glucosylceramide and sphingomyelin; the absence of laminated inclusion bodies (Zebra bodies) in glomerular epithelial cells; improvements in renal function; mitigation of hypohidrosis; the absence of angiokeratomas; and improvements in hearing abnormalities such as high frequency sensorineural hearing loss progressive hearing loss, sudden deafness, or tinnitus. Improvements in neurological symptoms include prevention of transient ischemic attack (TIA) or stroke; and amelioration of neuropathic pain manifesting itself as acroparaesthesia (burning or tingling in extremities). Another type of clinical marker that can be assessed for Fabry disease is the prevalence of deleterious cardiovascular manifestations. Common cardiac-related signs and symptoms of Fabry disease include left ventricular hypertrophy, valvular disease (especially mitral valve prolapse and/or regurgitation), premature coronary artery disease, angina, myocardial infarction, conduction abnormalities, arrhythmias, congestive heart failure.

[0070] The dose that achieves one or more of the aforementioned responses is a "therapeutically effective dose."

[0071] The phrase "pharmaceutically acceptable" refers to molecular entities and compositions that are physiologically tolerable and do not typically produce untoward reactions when administered to a human. In some embodiments, as used herein, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly in humans. The term "carrier" in reference to a pharmaceutical carrier refers to a diluent, adjuvant, excipient, or vehicle with which the compound is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils. Water or aqueous solution saline solutions and aqueous dextrose and glycerol solutions are preferably employed as carriers, particularly for injectable solutions. Suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin, 18th Edition, or other editions.

[0072] As used herein, the term "isolated" means that the referenced material is removed from the environment in which it is normally found. Thus, an isolated biological material can be free of cellular components, i.e., components of the cells in which the material is found or produced. In the case of nucleic acid molecules, an isolated nucleic acid includes a PCR product, an mRNA band on a gel, a cDNA, or a restriction fragment. In another embodiment, an isolated nucleic acid is preferably excised from the chromosome in which it may be found, and more preferably is no longer joined to non-regulatory, non-coding regions, or to other genes, located upstream or downstream of the gene contained by the isolated nucleic acid molecule when found in the chromosome. In yet another embodiment, the isolated nucleic acid lacks one or more introns. Isolated nucleic acids include sequences inserted into plasmids, cosmids, artificial chromosomes, and the like. Thus, in a specific embodiment, a recombinant nucleic acid is an isolated nucleic acid. An isolated protein may be associated with other proteins or nucleic acids, or both, with which it associates in the cell, or with cellular membranes if it is a membrane-associated protein. An isolated organelle, cell, or tissue is removed from the anatomical site in which it is found in an organism. An isolated material may be, but need not be, purified.

[0073] The terms "about" and "approximately" shall generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Typical, exemplary degrees of error are within 20 percent (%), preferably within 10%, and more preferably within 5% of a given value or range of values. Alternatively, and particularly

in biological systems, the terms "about" and "approximately" may mean values that are within an order of magnitude, preferably within 10- or 5-fold, and more preferably within 2-fold of a given value. Numerical quantities given herein are approximate unless stated otherwise, meaning that the term "about" or "approximately" can be inferred when not expressly stated.

[0074] The term "enzyme replacement therapy" or "ERT" refers to the introduction of a non-native, purified enzyme into an individual having a deficiency in such enzyme. The administered protein can be obtained from natural sources or by recombinant expression (as described in greater detail below). The term also refers to the introduction of a purified enzyme in an individual otherwise requiring or benefiting from administration of a purified enzyme, e.g., suffering from enzyme insufficiency. The introduced enzyme may be a purified, recombinant enzyme produced in vitro, or protein purified from isolated tissue or fluid, such as, e.g., placenta or animal milk, or from plants.

[0075] As used herein, the term "free base equivalent" or "FBE" refers to the amount of migalastat present in the migalastat or salt thereof. In other words, the term "FBE" means either an amount of migalastat free base, or the equivalent amount of migalastat free base that is provided by a salt of migalastat. For example, due to the weight of the hydrochloride salt, 150 mg of migalastat hydrochloride only provides as much migalastat as 123 mg of the free base form of migalastat. Other salts are expected to have different conversion factors, depending on the molecular weight of the salt.

[0076] The term "migalastat" encompasses migalastat free base or a pharmaceutically acceptable salt thereof (e.g., migalastat HCl), unless specifically indicated to the contrary.

[0077] The terms "mutation" and "variant" (e.g., as in "amenable mutation or variant") refer to a change in the nucleotide sequence of a gene or a chromosome. The two terms referred herein are typically used together – e.g., as in "mutation or variant"– referring to the change in nucleotide sequence stated in the previous sentence. If only one of the two terms is recited for some reason, the missing term was intended to be included and one should understand as such. Furthermore, the terms "amenable mutation" and "amenable variant" refer to a mutation or variant that is amenable to PC therapy, e.g. a mutation that is amenable to migalastat therapy. A particular type of amenable mutation or variant is a "HEK assay amenable mutation or variant", which is a mutation or variant that is determined to be amenable to migalastat therapy according to the criteria in the *in vitro* HEK assay described herein.

[0078] Fabry Disease

[0079] Fabry disease is a rare, progressive and devastating X-linked lysosomal storage disorder. Mutations in the GLA gene result in a deficiency of the lysosomal enzyme, α-Gal A, which is required for glycosphingolipid metabolism. Beginning early in life, the reduction in α-Gal A activity results in an accumulation of glycosphingolipids, including GL-3 and plasma lyso-Gb3, and leads to the symptoms and life-limiting sequelae of Fabry disease, including pain, gastrointestinal symptoms, renal failure, cardiomyopathy, cerebrovascular events, and early mortality. Early initiation of therapy and lifelong treatment provide an opportunity to slow disease progression and prolong life expectancy.

[0080] Fabry disease encompasses a spectrum of disease severity and age of onset, although it has traditionally been divided into 2 main phenotypes, "classic" and "late-onset". The classic phenotype has been ascribed primarily to males with undetectable to low α-Gal A activity and earlier onset of renal, cardiac and/or cerebrovascular manifestations. The late-onset phenotype has been ascribed primarily to males with higher residual α-Gal A activity and later onset of these disease manifestations. Heterozygous female carriers typically express the late-onset phenotype but depending on the pattern of X-chromosome inactivation may also display the classic phenotype.

[0081] More than 1,000 Fabry disease-causing GLA mutations have been identified. Approximately 60% are missense mutations, resulting in single amino acid substitutions in the α-Gal A enzyme. Missense GLA mutations often result in the production of abnormally folded and unstable forms of α-Gal A and the majority are associated with the classic phenotype. Normal cellular quality control mechanisms in the endoplasmic reticulum block the transit of these abnormal proteins to lysosomes and target them for premature degradation and elimination. Many missense mutant forms are targets for migalastat, an α-Gal A-specific pharmacological chaperone.

[0082] The clinical manifestations of Fabry disease span a broad spectrum of severity and roughly correlate with a patient's residual α-GAL levels. The majority of currently treated patients are referred to as classic Fabry disease patients, most of whom are males. These patients experience disease of various organs, including the kidneys, heart and brain, with disease symptoms first appearing in adolescence and typically progressing in severity until

death in the fourth or fifth decade of life. A number of recent studies suggest that there are a large number of undiagnosed males and females that have a range of Fabry disease symptoms, such as impaired cardiac or renal function and strokes, that usually first appear in adulthood. Individuals with this type of Fabry disease, referred to as late-onset Fabry disease, tend to have higher residual α-GAL levels than classic Fabry disease patients. Individuals with late-onset Fabry disease typically first experience disease symptoms in adulthood, and often have disease symptoms focused on a single organ, such as enlargement of the left ventricle or progressive kidney failure. In addition, late-onset Fabry disease may also present in the form of strokes of unknown cause.

[0083] Fabry patients have progressive kidney impairment, and untreated patients exhibit end-stage renal impairment by the fifth decade of life. Deficiency in α-Gal A activity leads to accumulation of GL-3 and related glycosphingolipids in many cell types including cells in the kidney. GL-3 accumulates in podocytes, epithelial cells and the tubular cells of the distal tubule and loop of Henle. Impairment in kidney function can manifest as proteinuria and reduced glomerular filtration rate.

[0084] Because Fabry disease is rare, involves multiple organs, has a wide age range of onset, and is heterogeneous, proper diagnosis is a challenge. Awareness is low among health care professionals and misdiagnoses are frequent. Diagnosis of Fabry disease is most often confirmed on the basis of decreased α-Gal A activity in plasma or peripheral leukocytes (WBCs) once a patient is symptomatic, coupled with mutational analysis. In females, diagnosis is even more challenging since the enzymatic identification of carrier females is less reliable due to random X-chromosomal inactivation in some cells of carriers. For example, some obligate carriers (daughters of classically affected males) have α-Gal A enzyme activities ranging from normal to very low activities. Since carriers can have normal α-Gal A enzyme activity in leukocytes, only the identification of an α-Gal A mutation by genetic testing provides precise carrier identification and/or diagnosis.

[0085] Also, as described above, the age of onset, progression, and severity of Fabry disease is at least partly dependent on the rate of substrate accumulation, which correlates to the enzymatic activity in lysosomes. Thus, a complete lack of residual activity can correspond to rapid substrate accumulation, and therefore a more severe form of the disease (having early onset and rapid progression). However, even small quantities of residual activity may be enough to degrade a large amounts of substrate. This in turn would lead to milder disease with

later onset and slower progression because of the slowed substrate accumulation. Considering these factors, it is thought that even modest increases in enzymatic activity can reduce the effect of a severe clinical phenotype. Data suggests that for most LSDs, just 1% to 6% of normal activity has been estimated as sufficient to delay or prevent disease onset or yield a more mild form of the disease. That is, just small increases in activity could have a significant impact on substrate levels, and hence disease severity and the rate of disease progression. Conversely, it is expected that a mutant lysosomal enzyme that shows no response in vitro would also not respond in vivo.

[0086] In one or more embodiments, mutant or variant forms of α-Gal A considered to be amenable to migalastat are defined as showing a relative increase (+10 μM migalastat) of ≥1.20-fold and an absolute increase (+ 10 μM migalastat) of ≥ 3.0% wild-type when the mutant form of α-Gal A is expressed in HEK-293 cells (referred to as the "HEK assay") according to Good Laboratory Practice (GLP)-validated in vitro assay (GLP HEK or Migalastat Amenability Assay). Such mutations or variants are also referred to herein as "HEK assay amenable" mutations or variants.

[0087] Previous screening methods have been provided that assess enzyme enhancement prior to the initiation of treatment. For example, an assay using HEK-293 cells has been utilized in clinical trials to predict whether a given mutation will be responsive to pharmacological chaperone (e.g., migalastat) treatment. In this assay, cDNA constructs are created. The corresponding α-Gal A mutant forms are transiently expressed in HEK-293 cells. Cells are then incubated ± migalastat (17 nM to 1 mM) for 4 to 5 days. After, α-Gal A levels are measured in cell lysates using a synthetic fluorogenic substrate (4-MU-α-Gal) or by western blot. This has been done for known disease-causing missense or small in-frame insertion/deletion mutations. Mutations that have previously been identified as responsive to a PC (e.g. migalastat) using these methods are listed in U.S. Pat. No. 8,592,362, which is hereby incorporated by reference in its entirety.

[0088] HEK assay amenable mutations include at least those mutations listed in a pharmacological reference table (e.g., the ones recited in the U.S. or International Product labels for a migalastat product such as GALAFOLD®). As used herein, "pharmacological reference table" refers to any publicly accessible written or electronic record, included in either the product label within the packaging of a migalastat product (e.g., GALAFOLD®) or in a website accessible by health care providers, that conveys whether a particular mutation or

variant is responsive to migalastat (e.g., GALAFOLD®) PC therapy, and is not necessarily limited to written records presented in tabular form. In one embodiment of the present invention, a "pharmacological reference table" thus refers to any depository of information that includes one or more amenable mutations or variants. In another embodiment, a "pharmacological reference table" refers to an updated depository of amenable mutations or variants that includes the novel mutations or variants disclosed herein (i.e., mutations presented in Table 2). An exemplary pharmacological reference table for HEK assay amenable mutations can be found in the summary of product characteristics and/or prescribing information for GALAFOLD® in various countries in which GALAFOLD® is approved for use, or at a website such as www.galafoldamenabilitytable.com or www.fabrygenevariantsearch.com, each of which is hereby incorporated by reference in its entirety.

[0089] An exemplary pharmacological reference table for HEK assay amenable mutations is provided in Table 1 below. In one or more embodiments, if a double mutation is present on the same chromosome (males and females), that patient is considered HEK assay amenable if the double mutation is present in one entry in Table 1 (e.g., D55V/Q57L). In some embodiments, if a double mutation is present on different chromosomes (only in females) that patient is considered HEK assay amenable if either one of the individual mutations is present in Table 1.

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.7C>G	c.C7G	L3V
c.8T>C	c.T8C	L3P
c.[11G>T; 620A>C]	c.G11T/A620C	R4M/Y207S
c.37G>A	c.G37A	A13T
c.37G>C	c.G37C	A13P
c.43G>A	c.G43A	A15T
c.44C>G	c.C44G	A15G
c.53T>G	c.T53G	F18C
c.58G>C	c.G58C	A20P
c.59C>A	c.C59A	A20D
c.65T>G	c.T65G	V22G
c.70T>C or c.70T>A	c.T70C or c.T70A	W24R
c.70T>G	c.T70G	W24G
c.72G>C or c.72G>T	c.G72C or c.G72T	W24C
c.95T>C	c.T95C	L32P
c.97G>C	c.G97C	D33H

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.97G>T	c.G97T	D33Y
c.98A>G	c.A98G	D33G
c.100A>G	c.A100G	N34D
c.100A>C	c.A100C	N34H
c.101A>C	c.A101C	N34T
c.101A>G	c.A101G	N34S
c.102T>G or c.102T>A	c.T102G or c.T102A	N34K
c.103G>C or c.103G>A	c.G103C or c.G103A	G35R
c.104G>A	c.G104A	G35E
c.104G>C	c.G104C	G35A
c.104G>T	c.G104T	G35V
c.107T>C	c.T107C	L36S
c.107T>G	c.T107G	L36W
c.108G>C or c.108G>T	c.G108C or c.G108T	L36F
c.109G>A	c.G109A	A37T
c.110C>T	c.C110T	A37V
c.122C>T	c.C122T	T41I
c.124A>C or c.124A>T	c.A124C or c.A124T	M42L
c.124A>G	c.A124G	M42V
c.125T>A	c.T125A	M42K
c.125T>C	c.T125C	M42T
c.125T>G	c.T125G	M42R
c.126G>A or c.126G>C or c.126G>T	c.G126A or c.G126C or c.G126T	M42I
c.137A>C	c.A137C	H46P
c.142G>C	c.G142C	E48Q
c.152T>A	c.T152A	M51K
c.153G>A or c.153G>T or c.153G>C	c.G153A or c.G153T or c.G153C	M51I
c.159C>G or c.159C>A	c.C159G or c.C159A	N53K
c.157A>G	c.A157G	N53D
c.[157A>C; 158A>T]	c.A157C/A158T	N53L
c.160C>T	c.C160T	L54F
c.161T>C	c.T161C	L54P
c.164A>G	c.A164G	D55G
c.164A>T	c.A164T	D55V
c.[164A>T; 170A>T]	c.A164T/A170T	D55V/Q57L
c.167G>T	c.G167T	C56F
c.167G>A	c.G167A	C56Y
c.170A>G	c.A170G	Q57R
c.170A>T	c.A170T	Q57L
c.175G>A	c.G175A	E59K
c.178C>A	c.C178A	P60T
c.178C>T	c.C178T	P60S
c.179C>T	c.C179T	P60L

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.184_185insTAG	c.184_185insTAG	S62delinsLA
c.196G>A	c.G196A	E66K
c.197A>G	c.A197G	E66G
c.207C>A or c.207C>G	c.C207A or c.C207G	F69L
c.214A>G	c.A214G	M72V
c.216G>A or c.216G>T or c.216G>C	c.G216A or c.G216T or c.G216C	M72I
c.218C>T	c.C218T	A73V
c.227T>C	c.T227C	M76T
c.239G>A	c.G239A	G80D
c.239G>T	c.G239T	G80V
c.247G>A	c.G247A	D83N
c.253G>A	c.G253A	G85S
c.254G>A	c.G254A	G85D
c.[253G>A; 254G>A]	c.G253A/G254A	G85N
c.[253G>A; 254G>T; 255T>G]	c.G253A/G254T/T255G	G85M
c.261G>C or c.261G>T	c.G261C or c.G261T	E87D
c.263A>C	c.A263C	Y88S
c.265C>T	c.C265T	L89F
c.272T>C	c.T272C	I91T
c.288G>A or c.288G>T or c.288G>C	c.G288A or c.G288T or c.G288C	M96I
c.286A>G	c.A286G	M96V
c.289G>C	c.G289C	A97P
c.290C>T	c.C290T	A97V
c.305C>T	c.C305T	S102L
c.311G>T	c.G311T	G104V
c.316C>T	c.C316T	L106F
c.320A>G	c.A320G	Q107R
c.322G>A	c.G322A	A108T
c.326A>G	c.A326G	D109G
c.334C>G	c.C334G	R112G
c.335G>A	c.G335A	R112H
c.335G>T	c.G335T	R112L
c.337T>A	c.T337A	F113I
c.337T>C or c.339T>A or c.339T>G	c.T337C or c.T339A or c.T339G	F113L
c.352C>T	c.C352T	R118C
c.361G>A	c.G361A	A121T
c.368A>G	c.A368G	Y123C
c.373C>T	c.C373T	H125Y
c.374A>T	c.A374T	H125L
c.376A>G	c.A376G	S126G
c.383G>A	c.G383A	G128E
c.399T>G	c.T399G	I133M

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.404C>T	c.C404T	A135V
c.408T>A or c.408T>G	c.T408A or c.T408G	D136E
c.416A>G	c.A416G	N139S
c.419A>C	c.A419C	K140T
c.427G>A	c.G427A	A143T
c.431G>A	c.G431A	G144D
c.431G>T	c.G431T	G144V
c.434T>C	c.T434C	F145S
c.436C>T	c.C436T	P146S
c.437C>G	c.C437G	P146R
c.454T>G	c.T454G	Y152D
c.454T>C	c.T454C	Y152H
c.455A>G	c.A455G	Y152C
c.465T>A or c.465T>G	c.T465A or c.T465G	D155E
c.466G>T	c.G466T	A156S
c.466G>A	c.G466A	A156T
c.467C>T	c.C467T	A156V
c.471G>C or c.471G>T	c.G471C or c.G471T	Q157H
c.484T>G	c.T484G	W162G
c.493G>C	c.G493C	D165H
c.494A>G	c.A494G	D165G
c.[496C>G; 497T>G]	c.C496G/T497G	L166G
c.496C>G	c.C496G	L166V
c.496_497delinsTC	c.496_497delinsTC	L166S
c.499C>G	c.C499G	L167V
c.506T>C	c.T506C	F169S
c.511G>A	c.G511A	G171S
c.520T>C	c.T520C	C174R
c.520T>G	c.T520G	C174G
c.525C>G or c.525C>A	c.C525G or c.C525A	D175E
c.539T>G	c.T539G	L180W
c.540G>C	c.G540C	L180F
c.548G>C	c.G548C	G183A
c.548G>A	c.G548A	G183D
c.550T>A	c.T550A	Y184N
c.551A>G	c.A551G	Y184C
c.553A>G	c.A553G	K185E
c.559A>G	c.A559G	M187V
c.559_564dup	c.559_564dup	p.M187_S188dup
c.560T>C	c.T560C	M187T
c.561G>T or c.561G>A or c.561G>C	c.G561T or c.G561A or c.G561C	M187I
c.567G>C or c.567G>T	c.G567C or c.G567T	L189F
c.572T>A	c.T572A	L191Q
c.580A>G	c.A580G	T194A

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.581C>T	c.C581T	T194I
c.584G>T	c.G584T	G195V
c.586A>G	c.A586G	R196G
c.593T>C	c.T593C	I198T
c.595G>A	c.G595A	V199M
c.596T>C	c.T596C	V199A
c.596T>G	c.T596G	V199G
c.599A>G	c.A599G	Y200C
c.602C>T	c.C602T	S201F
c.602C>A	c.C602A	S201Y
c.608A>T	c.A608T	E203V
c.609G>C or c.609G>T	c.G609C or c.G609T	E203D
c.610T>G	c.T610G	W204G
c.611G>T	c.G611T	W204L
c.613C>A	c.C613A	P205T
c.613C>T	c.C613T	P205S
c.614C>T	c.C614T	P205L
c.619T>C	c.T619C	Y207H
c.620A>C	c.A620C	Y207S
c.623T>G	c.T623G	M208R
c.628C>T	c.C628T	P210S
c.629C>T	c.C629T	P210L
c.638A>G	c.A638G	K213R
c.638A>T	c.A638T	K213M
c.640C>T	c.C640T	P214S
c.641C>T	c.C641T	P214L
c.643A>G	c.A643G	N215D
c.644A>G	c.A644G	N215S
c.644A>T	c.A644T	N215I
c.[644A>G; 937G>T]	c.A644G/G937T	N215S/D313Y
c.646T>G	c.T646G	Y216D
c.647A>C	c.A647C	Y216S
c.647A>G	c.A647G	Y216C
c.655A>C	c.A655C	I219L
c.656T>A	c.T656A	I219N
c.656T>C	c.T656C	I219T
c.659G>A	c.G659A	R220Q
c.659G>C	c.G659C	R220P
c.662A>C	c.A662C	Q221P
c.671A>C	c.A671C	N224T
c.671A>G	c.A671G	N224S
c.673C>G	c.C673G	H225D
c.682A>G	c.A682G	N228D
c.683A>G	c.A683G	N228S
c.687T>A or c.687T>G	c.T687A or c.T687G	F229L

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.695T>C	c.T695C	I232T
c.712A>G	c.A712G	S238G
c.713G>A	c.G713A	S238N
c.716T>C	c.T716C	I239T
c.717A>G	c.A717G	I239M
c.720G>C or c.720G>T	c.G720C or c.G720T	K240N
c.724A>G	c.A724G	I242V
c.724A>T	c.A724T	I242F
c.725T>A	c.T725A	I242N
c.725T>C	c.T725C	I242T
c.728T>G	c.T728G	L243W
c.729G>C or c.729G>T	c.G729C or c.G729T	L243F
c.730G>A	c.G730A	D244N
c.730G>C	c.G730C	D244H
c.733T>G	c.T733G	W245G
c.740C>G	c.C740G	S247C
c.747C>G or c.747C>A	c.C747G or c.C747A	N249K
c.748C>A	c.C748A	Q250K
c.749A>C	c.A749C	Q250P
c.749A>G	c.A749G	Q250R
c.750G>C	c.G750C	Q250H
c.758T>C	c.T758C	I253T
c.758T>G	c.T758G	I253S
c.760-762delGTT	c.760_762delGTT	p.V254del
c.769G>C	c.G769C	A257P
c.770C>T	c.C770T	A257V
c.770C>G	c.C770G	A257G
c.772G>C or c.772G>A	c.G772C or c.G772A	G258R
c.773G>T	c.G773T	G258V
c.776C>A	c.C776A	P259Q
c.776C>G	c.C776G	P259R
c.776C>T	c.C776T	P259L
c.779G>A	c.G779A	G260E
c.779G>C	c.G779C	G260A
c.781G>A	c.G781A	G261S
c.781G>C	c.G781C	G261R
c.781G>T	c.G781T	G261C
c.788A>G	c.A788G	N263S
c.790G>T	c.G790T	D264Y
c.794C>T	c.C794T	P265L
c.800T>C	c.T800C	M267T
c.805G>A	c.G805A	V269M
c.806T>C	c.T806C	V269A
c.809T>C	c.T809C	I270T
c.810T>G	c.T810G	I270M

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.811G>A	c.G811A	G271S
c.[811G>A; 937G>T]	c.G811A/G937T	G271S/D313Y
c.812G>A	c.G812A	G271D
c.823C>G	c.C823G	L275V
c.827G>A	c.G827A	S276N
c.829T>G	c.T829G	W277G
c.831G>T or c.831G>C	c.G831T or c.G831C	W277C
c.832A>T	c.A832T	N278Y
c.835C>G	c.C835G	Q279E
c.838C>A	c.C838A	Q280K
c.840A>T or c.840A>C	c.A840T or c.A840C	Q280H
c.844A>G	c.A844G	T282A
c.845C>T	c.C845T	T282I
c.850A>G	c.A850G	M284V
c.851T>C	c.T851C	M284T
c.860G>T	c.G860T	W287L
c.862G>C	c.G862C	A288P
c.866T>G	c.T866G	I289S
c.868A>C or c.868A>T	c.A868C or c.A868T	M290L
c.869T>C	c.T869C	M290T
c.870G>A or c.870G>C or c.870G>T	c.G870A or c.G870C or c.G870T	M290I
c.871G>A	c.G871A	A291T
c.877C>A	c.C877A	P293T
c.881T>C	c.T881C	L294S
c.884T>G	c.T884G	F295C
c.886A>G	c.A886G	M296V
c.886A>T or c.886A>C	c.A886T or c.A886C	M296L
c.887T>C	c.T887C	M296T
c.888G>A or c.888G>T or c.888G>C	c.G888A or c.G888T or c.G888C	M296I
c.893A>G	c.A893G	N298S
c.897C>G or c.897C>A	c.C897G or c.C897A	D299E
c.898C>T	c.C898T	L300F
c.899T>C	c.T899C	L300P
c.901C>G	c.C901G	R301G
c.902G>C	c.G902C	R301P
c.902G>A	c.G902A	R301Q
c.902G>T	c.G902T	R301L
c.907A>T	c.A907T	I303F
c.908T>A	c.T908A	I303N
c.911G>A	c.G911A	S304N
c.911G>C	c.G911C	S304T
c.919G>A	c.G919A	A307T
c.922A>G	c.A922G	K308E

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.924A>T or c.924A>C	c.A924T or c.A924C	K308N
c.925G>C	c.G925C	A309P
c.926C>T	c.C926T	A309V
c.928C>T	c.C928T	L310F
c.931C>G	c.C931G	L311V
c.935A>G	c.A935G	Q312R
c.936G>T or c.936G>C	c.G936T or c.G936C	Q312H
c.937G>T	c.G937T	D313Y
c.[937G>T; 1232G>A]	c.G937T/G1232A	D313Y/G411D
c.938A>G	c.A938G	D313G
c.946G>A	c.G946A	V316I
c.947T>G	c.T947G	V316G
c.950T>C	c.T950C	I317T
c.955A>T	c.A955T	I319F
c.956T>C	c.T956C	I319T
c.958A>C	c.A958C	N320H
c.959A>T	c.A959T	N320I
c.962A>G	c.A962G	Q321R
c.962A>T	c.A962T	Q321L
c.963G>C or c.963G>T	c.G963C or c.G963T	Q321H
c.964G>A	c.G964A	D322N
c.964G>C	c.G964C	D322H
c.966C>A or c.966C>G	c.C966A or c.C966G	D322E
c.967C>A	c.C967A	P323T
c.968C>G	c.C968G	P323R
c.973G>A	c.G973A	G325S
c.973G>C	c.G973C	G325R
c.978G>C or c.978G>T	c.G978C or c.G978T	K326N
c.979C>G	c.C979G	Q327E
c.980A>T	c.A980T	Q327L
c.983G>C	c.G983C	G328A
c.989A>C	c.A989C	Q330P
c.989A>G	c.A989G	Q330R
c.1001G>A	c.G1001A	G334E
c.1010T>C	c.T1010C	F337S
c.1012G>A	c.G1012A	E338K
c.1013A>T	c.A1013T	E338V
c.1016T>C	c.T1016C	V339A
c.1016T>A	c.T1016A	V339E
c.1027C>A	c.C1027A	P343T
c.1028C>T	c.C1028T	P343L
c.1033T>C	c.T1033C	S345P
c.1046G>C	c.G1046C	W349S
c.1055C>G	c.C1055G	A352G
c.1055C>T	c.C1055T	A352V

Table 1

Nucleotide change	Nucleotide change	Protein sequence change
c.1061T>A	c.T1061A	I354K
c.1066C>G	c.C1066G	R356G
c.1066C>T	c.C1066T	R356W
c.1067G>A	c.G1067A	R356Q
c.1067G>C	c.G1067C	R356P
c.1072G>C	c.G1072C	E358Q
c.1073A>C	c.A1073C	E358A
c.1073A>G	c.A1073G	E358G
c.1074G>T or c.1074G>C	c.G1074T or c.G1074C	E358D
c.1076T>C	c.T1076C	I359T
c.1078G>A	c.G1078A	G360S
c.1078G>T	c.G1078T	G360C
c.1079G>A	c.G1079A	G360D
c.1082G>A	c.G1082A	G361E
c.1082G>C	c.G1082C	G361A
c.1084C>A	c.C1084A	P362T
c.1085C>T	c.C1085T	P362L
c.1087C>T	c.C1087T	R363C
c.1088G>A	c.G1088A	R363H
c.1102G>A	c.G1102A	A368T
c.1117G>A	c.G1117A	G373S
c.1124G>A	c.G1124A	G375E
c.1139C>T	c.C1139T	P380L
c.1153A>G	c.A1153G	T385A
c.1168G>A	c.G1168A	V390M
c.1171A>G	c.A1171G	K391E
c.1172A>C	c.A1172C	K391T
c.1175G>C	c.G1175C	R392T
c.1184G>A	c.G1184A	G395E
c.1184G>C	c.G1184C	G395A
c.1192G>A	c.G1192A	E398K
c.1202_1203insGACTTC	c.1202_1203insGACTTC	p.T400_S401dup
c.1208T>C	c.T1208C	L403S
c.1222A>T	c.A1222T	N408Y
c.1225C>G	c.C1225G	P409A
c.1225C>T	c.C1225T	P409S
c.1225C>A	c.C1225A	P409T
c.1228A>G	c.A1228G	T410A
c.1229C>T	c.C1229T	T410I
c.1232G>A	c.G1232A	G411D
c.1234A>C	c.A1234C	T412P
c.1235C>A	c.C1235A	T412N
c.1253A>G	c.A1253G	E418G
c.1261A>G	c.A1261G	M421V

[0090] However, as only certain mutations are amenable to treatment with migalastat, there is a need to identify new mutations and determine whether such mutations are amenable to migalastat therapy. As described in the Example below, several new mutations have been identified and determined to be mutations that are amenable to migalastat therapy.

[0091] As described above, α-Gal A refers to an enzyme encoded by the human GLA gene. The coding sequence of the GLA gene consists of 1287 nucleotides. The human α-Gal A enzyme consists of 429 amino acid residues. To create a list of all possible non-synonymous missense mutations for GLA, each nucleotide on the coding sequence was individually replaced on the coding sequence with the other 3 nucleotides, and the effect of each substitution on the protein sequence was examined.

[0092] If the codon change led to a change in the protein sequence by a single amino acid residue substitution and that amino acid substitution had not been identified previously, the mutation was recorded and tested with a HEK assay. Those mutations which were found to be HEK assay amenable were labelled as prophetic amenable mutations. When multiple different nucleotide changes within a single codon lead to the same amino acid residue substitution on that position, the protein sequence change was listed as a single entry with alternative nucleotide changes.

[0093] The prophetic amenable mutations identified include N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, L10Q, L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, R17P, R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, G28R, G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, R38W, T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V, N53H, N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, P60R, D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, L68I, F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, L75F, L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E,

K82M, K82N, K82R, K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, I91F, I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, D101V, S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, D109A, D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, H125D, H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, D136N, D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, G144A, G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, Y151D, Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, F159V, F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, F169L, F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, E178A, E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, H186D, H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, L191V, N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, S197I, S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, L206V, Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, N215H, N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, I219M, I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, F229Y, A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C,

S238I, S238T, I239L, K240E, K240M, K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, T246R, S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, E251V, R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, P259A, P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, L275I, W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, L286V, A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, N298T, D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, K308Q, K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, D315Y, V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, G325V, K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E, Q330H, Q330K, L331H, L331P, L331R, L331V, R332G, R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, F337L, F337V, F337Y, E338A, E338D, E338G, V339M, E341A, E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, W349C, W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, I359F, I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, T366P, T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, G373C, K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, P380R, P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, L388R, L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N,

K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, F396L, F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, R402M, R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, N408T, P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, E418A, E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, M423L, M423T, S424L, L425F, D427N, and L429R. These mutations are also presented in Table 2 with their corresponding nucleotide changes.

[0094] Accordingly, in one or more embodiments, migalastat is used to treat Fabry disease and/or enhance α-Gal A activity in a patient having an α-Gal A mutation selected from the group consisting of the mutations presented in Table 2. In various embodiments, these α-Gal A mutations are relative to the amino acid sequence shown in SEQ ID NO: 2.

[0095] Exemplary nucleotide changes associated with these novel mutations are shown in Table 2 below:

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.13A>G	c.A13G	N5D	p.(Asn5Asp)
c.15C>G	c.C15G	N5K	p.(Asn5Lys)
c.17C>T	c.C17T	P6L	p.(Pro6Leu)
c.17C>A	c.C17A	P6Q	p.(Pro6Gln)
c.17C>G	c.C17G	P6R	p.(Pro6Arg)
c.16C>T	c.C16T	P6S	p.(Pro6Ser)
c.16C>A	c.C16A	P6T	p.(Pro6Thr)
c.21A>T	c.A21T	E7D	p.(Glu7Asp)
c.19G>A	c.G19A	E7K	p.(Glu7Lys)
c.20A>T	c.A20T	E7V	p.(Glu7Val)
c.22C>A	c.C22A	L8I	p.(Leu8Ile)
c.23T>C	c.T23C	L8P	p.(Leu8Pro)
c.23T>A	c.T23A	L8Q	p.(Leu8Gln)
c.26A>T	c.A26T	H9L	p.(His9Leu)
c.27T>A	c.T27A	H9Q	p.(His9Gln)
c.26A>G	c.A26G	H9R	p.(His9Arg)
c.25C>T	c.C25T	H9Y	p.(His9Tyr)
c.28C>A	c.C28A	L10M	p.(Leu10Met)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.29T>C	c.T29C	L10P	p.(Leu10Pro)
c.29T>A	c.T29A	L10Q	p.(Leu10Gln)
c.29T>G	c.T29G	L10R	p.(Leu10Arg)
c.28C>G	c.C28G	L10V	p.(Leu10Val)
c.31G>T	c.G31T	G11C	p.(Gly11Cys)
c.32G>A	c.G32A	G11D	p.(Gly11Asp)
c.31G>C	c.G31C	G11R	p.(Gly11Arg)
c.31G>A	c.G31A	G11S	p.(Gly11Ser)
c.32G>T	c.G32T	G11V	p.(Gly11Val)
c.34T>G	c.T34G	C12G	p.(Cys12Gly)
c.34T>C	c.T34C	C12R	p.(Cys12Arg)
c.34T>A	c.T34A	C12S	p.(Cys12Ser)
c.35G>A	c.G35A	C12Y	p.(Cys12Tyr)
c.38C>A	c.C38A	A13E	p.(Ala13Glu)
c.38C>G	c.C38G	A13G	p.(Ala13Gly)
c.40C>T	c.C40T	L14F	p.(Leu14Phe)
c.41T>A	c.T41A	L14H	p.(Leu14His)
c.40C>G	c.C40G	L14V	p.(Leu14Val)
c.49C>T	c.C49T	R17C	p.(Arg17Cys)
c.49C>G	c.C49G	R17G	p.(Arg17Gly)
c.50G>A	c.G50A	R17H	p.(Arg17His)
c.50G>C	c.G50C	R17P	p.(Arg17Pro)
c.49C>A	c.C49A	R17S	p.(Arg17Ser)
c.52T>A	c.T52A	F18I	p.(Phe18Ile)
c.54C>G	c.C54G	F18L	p.(Phe18Leu)
c.59C>G	c.C59G	A20G	p.(Ala20Gly)
c.62T>A	c.T62A	L21H	p.(Leu21His)
c.65T>C	c.T65C	V22A	p.(Val22Ala)
c.64G>T	c.G64T	V22F	p.(Val22Phe)
c.64G>A	c.G64A	V22I	p.(Val22Ile)
c.64G>C	c.G64C	V22L	p.(Val22Leu)
c.67T>C	c.T67C	S23P	p.(Ser23Pro)
c.67T>A	c.T67A	S23T	p.(Ser23Thr)
c.71G>C	c.G71C	W24S	p.(Trp24Ser)
c.73G>C	c.G73C	D25H	p.(Asp25His)
c.77T>A	c.T77A	I26N	p.(Ile26Asn)
c.79C>G	c.C79G	P27A	p.(Pro27Ala)
c.80C>T	c.C80T	P27L	p.(Pro27Leu)
c.79C>T	c.C79T	P27S	p.(Pro27Ser)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.79C>A	c.C79A	P27T	p.(Pro27Thr)
c.83G>A	c.G83A	G28E	p.(Gly28Glu)
c.82G>C	c.G82C	G28R	p.(Gly28Arg)
c.82G>T	c.G82T	G28W	p.(Gly28Trp)
c.86C>G	c.C86G	A29G	p.(Ala29Gly)
c.85G>C	c.G85C	A29P	p.(Ala29Pro)
c.86C>T	c.C86T	A29V	p.(Ala29Val)
c.88A>G	c.A88G	R30G	p.(Arg30Gly)
c.94C>A	c.C94A	L32M	p.(Leu32Met)
c.95T>A	c.T95A	L32Q	p.(Leu32Gln)
c.95T>G	c.T95G	L32R	p.(Leu32Arg)
c.94C>G	c.C94G	L32V	p.(Leu32Val)
c.98A>C	c.A98C	D33A	p.(Asp33Ala)
c.99C>G	c.C99G	D33E	p.(Asp33Glu)
c.98A>T	c.A98T	D33V	p.(Asp33Val)
c.106T>A	c.T106A	L36M	p.(Leu36Met)
c.106T>G	c.T106G	L36V	p.(Leu36Val)
c.110C>A	c.C110A	A37E	p.(Ala37Glu)
c.110C>G	c.C110G	A37G	p.(Ala37Gly)
c.109G>T	c.G109T	A37S	p.(Ala37Ser)
c.112A>G	c.A112G	R38G	p.(Arg38Gly)
c.113G>T	c.G113T	R38M	p.(Arg38Met)
c.112A>T	c.A112T	R38W	p.(Arg38Trp)
c.115A>G	c.A115G	T39A	p.(Thr39Ala)
c.116C>A	c.C116A	T39K	p.(Thr39Lys)
c.116C>T	c.C116T	T39M	p.(Thr39Met)
c.116C>G	c.C116G	T39R	p.(Thr39Arg)
c.115A>T	c.A115T	T39S	p.(Thr39Ser)
c.121A>G	c.A121G	T41A	p.(Thr41Ala)
c.122C>A	c.C122A	T41N	p.(Thr41Asn)
c.121A>T	c.A121T	T41S	p.(Thr41Ser)
c.128G>C	c.G128C	G43A	p.(Gly43Ala)
c.133C>A	c.C133A	L45M	p.(Leu45Met)
c.133C>G	c.C133G	L45V	p.(Leu45Val)
c.136C>G	c.C136G	H46D	p.(His46Asp)
c.136C>A	c.C136A	H46N	p.(His46Asn)
c.138C>G	c.C138G	H46Q	p.(His46Gln)
c.143A>C	c.A143C	E48A	p.(Glu48Ala)
c.149T>A	c.T149A	F50Y	p.(Phe50Tyr)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.152T>G	c.T152G	M51R	p.(Met51Arg)
c.152T>C	c.T152C	M51T	p.(Met51Thr)
c.151A>G	c.A151G	M51V	p.(Met51Val)
c.157A>C	c.A157C	N53H	p.(Asn53His)
c.158A>T	c.A158T	N53I	p.(Asn53Ile)
c.158A>G	c.A158G	N53S	p.(Asn53Ser)
c.158A>C	c.A158C	N53T	p.(Asn53Thr)
c.161T>A	c.T161A	L54H	p.(Leu54His)
c.161T>G	c.T161G	L54R	p.(Leu54Arg)
c.160C>G	c.C160G	L54V	p.(Leu54Val)
c.164A>C	c.A164C	D55A	p.(Asp55Ala)
c.165C>G	c.C165G	D55E	p.(Asp55Glu)
c.163G>C	c.G163C	D55H	p.(Asp55His)
c.163G>T	c.G163T	D55Y	p.(Asp55Tyr)
c.168C>G	c.C168G	C56W	p.(Cys56Trp)
c.172G>A	c.G172A	E58K	p.(Glu58Lys)
c.176A>C	c.A176C	E59A	p.(Glu59Ala)
c.177G>C	c.G177C	E59D	p.(Glu59Asp)
c.176A>G	c.A176G	E59G	p.(Glu59Gly)
c.175G>C	c.G175C	E59Q	p.(Glu59Gln)
c.176A>T	c.A176T	E59V	p.(Glu59Val)
c.178C>G	c.C178G	P60A	p.(Pro60Ala)
c.179C>A	c.C179A	P60Q	p.(Pro60Gln)
c.179C>G	c.C179G	P60R	p.(Pro60Arg)
c.183T>A	c.T183A	D61E	p.(Asp61Glu)
c.182A>T	c.A182T	D61V	p.(Asp61Val)
c.184T>G	c.T184G	S62A	p.(Ser62Ala)
c.185C>G	c.C185G	S62C	p.(Ser62Cys)
c.185C>T	c.C185T	S62F	p.(Ser62Phe)
c.184T>C	c.T184C	S62P	p.(Ser62Pro)
c.185C>A	c.C185A	S62Y	p.(Ser62Tyr)
c.190A>C	c.A190C	I64L	p.(Ile64Leu)
c.190A>G	c.A190G	I64V	p.(Ile64Val)
c.193A>T	c.A193T	S65C	p.(Ser65Cys)
c.193A>G	c.A193G	S65G	p.(Ser65Gly)
c.195T>A	c.T195A	S65R	p.(Ser65Arg)
c.198G>C	c.G198C	E66D	p.(Glu66Asp)
c.197A>T	c.A197T	E66V	p.(Glu66Val)
c.199A>G	c.A199G	K67E	p.(Lys67Glu)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.200A>T	c.A200T	K67M	p.(Lys67Met)
c.201G>C	c.G201C	K67N	p.(Lys67Asn)
c.199A>C	c.A199C	K67Q	p.(Lys67Gln)
c.200A>C	c.A200C	K67T	p.(Lys67Thr)
c.202C>A	c.C202A	L68I	p.(Leu68Ile)
c.205T>A	c.T205A	F69I	p.(Phe69Ile)
c.206T>A	c.T206A	F69Y	p.(Phe69Tyr)
c.210G>C	c.G210C	M70I	p.(Met70Ile)
c.209T>A	c.T209A	M70K	p.(Met70Lys)
c.208A>T	c.A208T	M70L	p.(Met70Leu)
c.209T>G	c.T209G	M70R	p.(Met70Arg)
c.212A>C	c.A212C	E71A	p.(Glu71Ala)
c.213G>C	c.G213C	E71D	p.(Glu71Asp)
c.212A>G	c.A212G	E71G	p.(Glu71Gly)
c.211G>C	c.G211C	E71Q	p.(Glu71Gln)
c.212A>T	c.A212T	E71V	p.(Glu71Val)
c.214A>T	c.A214T	M72L	p.(Met72Leu)
c.215T>C	c.T215C	M72T	p.(Met72Thr)
c.217G>T	c.G217T	A73S	p.(Ala73Ser)
c.217G>A	c.G217A	A73T	p.(Ala73Thr)
c.222G>C	c.G222C	E74D	p.(Glu74Asp)
c.221A>G	c.A221G	E74G	p.(Glu74Gly)
c.220G>A	c.G220A	E74K	p.(Glu74Lys)
c.221A>T	c.A221T	E74V	p.(Glu74Val)
c.223C>T	c.C223T	L75F	p.(Leu75Phe)
c.224T>C	c.T224C	L75P	p.(Leu75Pro)
c.226A>G	c.A226G	M76V	p.(Met76Val)
c.229G>A	c.G229A	V77I	p.(Val77Ile)
c.229G>C	c.G229C	V77L	p.(Val77Leu)
c.233C>T	c.C233T	S78L	p.(Ser78Leu)
c.232T>C	c.T232C	S78P	p.(Ser78Pro)
c.236A>C	c.A236C	E79A	p.(Glu79Ala)
c.237A>T	c.A237T	E79D	p.(Glu79Asp)
c.236A>G	c.A236G	E79G	p.(Glu79Gly)
c.235G>A	c.G235A	E79K	p.(Glu79Lys)
c.235G>C	c.G235C	E79Q	p.(Glu79Gln)
c.236A>T	c.A236T	E79V	p.(Glu79Val)
c.239G>C	c.G239C	G80A	p.(Gly80Ala)
c.238G>T	c.G238T	G80C	p.(Gly80Cys)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.238G>A	c.G238A	G80S	p.(Gly80Ser)
c.242G>T	c.G242T	W81L	p.(Trp81Leu)
c.244A>G	c.A244G	K82E	p.(Lys82Glu)
c.245A>T	c.A245T	K82M	p.(Lys82Met)
c.246G>C	c.G246C	K82N	p.(Lys82Asn)
c.245A>G	c.A245G	K82R	p.(Lys82Arg)
c.245A>C	c.A245C	K82T	p.(Lys82Thr)
c.248A>C	c.A248C	D83A	p.(Asp83Ala)
c.249T>A	c.T249A	D83E	p.(Asp83Glu)
c.248A>G	c.A248G	D83G	p.(Asp83Gly)
c.248A>T	c.A248T	D83V	p.(Asp83Val)
c.251C>A	c.C251A	A84E	p.(Ala84Glu)
c.251C>G	c.C251G	A84G	p.(Ala84Gly)
c.250G>C	c.G250C	A84P	p.(Ala84Pro)
c.250G>T	c.G250T	A84S	p.(Ala84Ser)
c.250G>A	c.G250A	A84T	p.(Ala84Thr)
c.251C>T	c.C251T	A84V	p.(Ala84Val)
c.254G>C	c.G254C	G85A	p.(Gly85Ala)
c.253G>T	c.G253T	G85C	p.(Gly85Cys)
c.253G>C	c.G253C	G85R	p.(Gly85Arg)
c.257A>T	c.A257T	Y86F	p.(Tyr86Phe)
c.260A>G	c.A260G	E87G	p.(Glu87Gly)
c.262T>C	c.T262C	Y88H	p.(Tyr88His)
c.262T>A	c.T262A	Y88N	p.(Tyr88Asn)
c.265C>G	c.C265G	L89V	p.(Leu89Val)
c.271A>T	c.A271T	I91F	p.(Ile91Phe)
c.271A>C	c.A271C	I91L	p.(Ile91Leu)
c.273T>G	c.T273G	I91M	p.(Ile91Met)
c.272T>G	c.T272G	I91S	p.(Ile91Ser)
c.286A>T	c.A286T	M96L	p.(Met96Leu)
c.287T>C	c.T287C	M96T	p.(Met96Thr)
c.290C>A	c.C290A	A97D	p.(Ala97Asp)
c.289G>T	c.G289T	A97S	p.(Ala97Ser)
c.289G>A	c.G289A	A97T	p.(Ala97Thr)
c.293C>A	c.C293A	P98H	p.(Pro98His)
c.293C>T	c.C293T	P98L	p.(Pro98Leu)
c.293C>G	c.C293G	P98R	p.(Pro98Arg)
c.295C>G	c.C295G	Q99E	p.(Gln99Glu)
c.296A>T	c.A296T	Q99L	p.(Gln99Leu)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.296A>C	c.A296C	Q99P	p.(Gln99Pro)
c.296A>G	c.A296G	Q99R	p.(Gln99Arg)
c.302A>C	c.A302C	D101A	p.(Asp101Ala)
c.303T>A	c.T303A	D101E	p.(Asp101Glu)
c.302A>G	c.A302G	D101G	p.(Asp101Gly)
c.301G>C	c.G301C	D101H	p.(Asp101His)
c.302A>T	c.A302T	D101V	p.(Asp101Val)
c.304T>G	c.T304G	S102A	p.(Ser102Ala)
c.304T>C	c.T304C	S102P	p.(Ser102Pro)
c.304T>A	c.T304A	S102T	p.(Ser102Thr)
c.311G>C	c.G311C	G104A	p.(Gly104Ala)
c.311G>A	c.G311A	G104D	p.(Gly104Asp)
c.310G>A	c.G310A	G104S	p.(Gly104Ser)
c.313A>G	c.A313G	R105G	p.(Arg105Gly)
c.314G>T	c.G314T	R105I	p.(Arg105Ile)
c.314G>A	c.G314A	R105K	p.(Arg105Lys)
c.314G>C	c.G314C	R105T	p.(Arg105Thr)
c.317T>A	c.T317A	L106H	p.(Leu106His)
c.316C>A	c.C316A	L106I	p.(Leu106Ile)
c.317T>C	c.T317C	L106P	p.(Leu106Pro)
c.316C>G	c.C316G	L106V	p.(Leu106Val)
c.319C>G	c.C319G	Q107E	p.(Gln107Glu)
c.321G>C	c.G321C	Q107H	p.(Gln107His)
c.319C>A	c.C319A	Q107K	p.(Gln107Lys)
c.323C>A	c.C323A	A108E	p.(Ala108Glu)
c.323C>T	c.C323T	A108V	p.(Ala108Val)
c.326A>C	c.A326C	D109A	p.(Asp109Ala)
c.327C>G	c.C327G	D109E	p.(Asp109Glu)
c.325G>C	c.G325C	D109H	p.(Asp109His)
c.325G>A	c.G325A	D109N	p.(Asp109Asn)
c.325G>T	c.G325T	D109Y	p.(Asp109Tyr)
c.328C>A	c.C328A	P110T	p.(Pro110Thr)
c.337T>G	c.T337G	F113V	p.(Phe113Val)
c.338T>A	c.T338A	F113Y	p.(Phe113Tyr)
c.341C>T	c.C341T	P114L	p.(Pro114Leu)
c.343C>G	c.C343G	H115D	p.(His115Asp)
c.343C>A	c.C343A	H115N	p.(His115Asn)
c.346G>C	c.G346C	G116R	p.(Gly116Arg)
c.351T>G	c.T351G	I117M	p.(Ile117Met)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.350T>C	c.T350C	I117T	p.(Ile117Thr)
c.362C>T	c.C362T	A121V	p.(Ala121Val)
c.367T>G	c.T367G	Y123D	p.(Tyr123Asp)
c.368A>T	c.A368T	Y123F	p.(Tyr123Phe)
c.367T>A	c.T367A	Y123N	p.(Tyr123Asn)
c.368A>C	c.A368C	Y123S	p.(Tyr123Ser)
c.370G>A	c.G370A	V124I	p.(Val124Ile)
c.373C>G	c.C373G	H125D	p.(His125Asp)
c.373C>A	c.C373A	H125N	p.(His125Asn)
c.374A>G	c.A374G	H125R	p.(His125Arg)
c.376A>T	c.A376T	S126C	p.(Ser126Cys)
c.377G>T	c.G377T	S126I	p.(Ser126Ile)
c.379A>G	c.A379G	K127E	p.(Lys127Glu)
c.383G>C	c.G383C	G128A	p.(Gly128Ala)
c.385C>G	c.C385G	L129V	p.(Leu129Val)
c.389A>T	c.A389T	K130M	p.(Lys130Met)
c.390G>C	c.G390C	K130N	p.(Lys130Asn)
c.388A>C	c.A388C	K130Q	p.(Lys130Gln)
c.391C>G	c.C391G	L131V	p.(Leu131Val)
c.397A>C	c.A397C	I133L	p.(Ile133Leu)
c.398T>C	c.T398C	I133T	p.(Ile133Thr)
c.397A>G	c.A397G	I133V	p.(Ile133Val)
c.404C>A	c.C404A	A135E	p.(Ala135Glu)
c.404C>G	c.C404G	A135G	p.(Ala135Gly)
c.403G>T	c.G403T	A135S	p.(Ala135Ser)
c.403G>A	c.G403A	A135T	p.(Ala135Thr)
c.407A>C	c.A407C	D136A	p.(Asp136Ala)
c.406G>A	c.G406A	D136N	p.(Asp136Asn)
c.407A>T	c.A407T	D136V	p.(Asp136Val)
c.410T>C	c.T410C	V137A	p.(Val137Ala)
c.410T>A	c.T410A	V137D	p.(Val137Asp)
c.410T>G	c.T410G	V137G	p.(Val137Gly)
c.409G>A	c.G409A	V137I	p.(Val137Ile)
c.409G>C	c.G409C	V137L	p.(Val137Leu)
c.413G>C	c.G413C	G138A	p.(Gly138Ala)
c.415A>C	c.A415C	N139H	p.(Asn139His)
c.416A>T	c.A416T	N139I	p.(Asn139Ile)
c.417T>A	c.T417A	N139K	p.(Asn139Lys)
c.415A>T	c.A415T	N139Y	p.(Asn139Tyr)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.418A>G	c.A418G	K140E	p.(Lys140Glu)
c.419A>T	c.A419T	K140I	p.(Lys140Ile)
c.420A>T	c.A420T	K140N	p.(Lys140Asn)
c.418A>C	c.A418C	K140Q	p.(Lys140Gln)
c.419A>G	c.A419G	K140R	p.(Lys140Arg)
c.421A>T	c.A421T	T141S	p.(Thr141Ser)
c.428C>A	c.C428A	A143E	p.(Ala143Glu)
c.428C>G	c.C428G	A143G	p.(Ala143Gly)
c.431G>C	c.G431C	G144A	p.(Gly144Ala)
c.430G>T	c.G430T	G144C	p.(Gly144Cys)
c.430G>C	c.G430C	G144R	p.(Gly144Arg)
c.430G>A	c.G430A	G144S	p.(Gly144Ser)
c.434T>G	c.T434G	F145C	p.(Phe145Cys)
c.435C>G	c.C435G	F145L	p.(Phe145Leu)
c.433T>G	c.T433G	F145V	p.(Phe145Val)
c.434T>A	c.T434A	F145Y	p.(Phe145Tyr)
c.436C>G	c.C436G	P146A	p.(Pro146Ala)
c.437C>A	c.C437A	P146H	p.(Pro146His)
c.437C>T	c.C437T	P146L	p.(Pro146Leu)
c.436C>A	c.C436A	P146T	p.(Pro146Thr)
c.440G>C	c.G440C	G147A	p.(Gly147Ala)
c.442A>T	c.A442T	S148C	p.(Ser148Cys)
c.442A>G	c.A442G	S148G	p.(Ser148Gly)
c.443G>C	c.G443C	S148T	p.(Ser148Thr)
c.446T>G	c.T446G	F149C	p.(Phe149Cys)
c.449G>A	c.G449A	G150E	p.(Gly150Glu)
c.449G>T	c.G449T	G150V	p.(Gly150Val)
c.452A>G	c.A452G	Y151C	p.(Tyr151Cys)
c.451T>G	c.T451G	Y151D	p.(Tyr151Asp)
c.452A>C	c.A452C	Y151S	p.(Tyr151Ser)
c.455A>T	c.A455T	Y152F	p.(Tyr152Phe)
c.455A>C	c.A455C	Y152S	p.(Tyr152Ser)
c.458A>C	c.A458C	D153A	p.(Asp153Ala)
c.457G>C	c.G457C	D153H	p.(Asp153His)
c.457G>A	c.G457A	D153N	p.(Asp153Asn)
c.458A>T	c.A458T	D153V	p.(Asp153Val)
c.457G>T	c.G457T	D153Y	p.(Asp153Tyr)
c.467C>G	c.C467G	A156G	p.(Ala156Gly)
c.469C>G	c.C469G	Q157E	p.(Gln157Glu)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.469C>A	c.C469A	Q157K	p.(Gln157Lys)
c.470A>T	c.A470T	Q157L	p.(Gln157Leu)
c.470A>C	c.A470C	Q157P	p.(Gln157Pro)
c.472A>G	c.A472G	T158A	p.(Thr158Ala)
c.473C>T	c.C473T	T158I	p.(Thr158Ile)
c.473C>A	c.C473A	T158N	p.(Thr158Asn)
c.472A>T	c.A472T	T158S	p.(Thr158Ser)
c.475T>A	c.T475A	F159I	p.(Phe159Ile)
c.477T>A	c.T477A	F159L	p.(Phe159Leu)
c.475T>G	c.T475G	F159V	p.(Phe159Val)
c.476T>A	c.T476A	F159Y	p.(Phe159Tyr)
c.479C>G	c.C479G	A160G	p.(Ala160Gly)
c.478G>T	c.G478T	A160S	p.(Ala160Ser)
c.478G>A	c.G478A	A160T	p.(Ala160Thr)
c.479C>T	c.C479T	A160V	p.(Ala160Val)
c.481G>C	c.G481C	D161H	p.(Asp161His)
c.481G>A	c.G481A	D161N	p.(Asp161Asn)
c.482A>T	c.A482T	D161V	p.(Asp161Val)
c.481G>T	c.G481T	D161Y	p.(Asp161Tyr)
c.485G>C	c.G485C	W162S	p.(Trp162Ser)
c.491T>C	c.T491C	V164A	p.(Val164Ala)
c.490G>A	c.G490A	V164I	p.(Val164Ile)
c.490G>C	c.G490C	V164L	p.(Val164Leu)
c.494A>C	c.A494C	D165A	p.(Asp165Ala)
c.495T>A	c.T495A	D165E	p.(Asp165Glu)
c.496C>A	c.C496A	L166M	p.(Leu166Met)
c.497T>A	c.T497A	L166Q	p.(Leu166Gln)
c.499C>A	c.C499A	L167I	p.(Leu167Ile)
c.506T>G	c.T506G	F169C	p.(Phe169Cys)
c.507T>A	c.T507A	F169L	p.(Phe169Leu)
c.505T>G	c.T505G	F169V	p.(Phe169Val)
c.506T>A	c.T506A	F169Y	p.(Phe169Tyr)
c.512G>C	c.G512C	G171A	p.(Gly171Ala)
c.512G>T	c.G512T	G171V	p.(Gly171Val)
c.518A>G	c.A518G	Y173C	p.(Tyr173Cys)
c.518A>T	c.A518T	Y173F	p.(Tyr173Phe)
c.517T>C	c.T517C	Y173H	p.(Tyr173His)
c.518A>C	c.A518C	Y173S	p.(Tyr173Ser)
c.524A>G	c.A524G	D175G	p.(Asp175Gly)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.523G>C	c.G523C	D175H	p.(Asp175His)
c.524A>T	c.A524T	D175V	p.(Asp175Val)
c.523G>T	c.G523T	D175Y	p.(Asp175Tyr)
c.526A>T	c.A526T	S176C	p.(Ser176Cys)
c.528T>A or c.528T>G	c.T528A or c.T528G	S176R	p.(Ser176Arg)
c.531G>C	c.G531C	L177F	p.(Leu177Phe)
c.529T>A	c.T529A	L177M	p.(Leu177Met)
c.530T>C	c.T530C	L177S	p.(Leu177Ser)
c.529T>G	c.T529G	L177V	p.(Leu177Val)
c.530T>G	c.T530G	L177W	p.(Leu177Trp)
c.533A>C	c.A533C	E178A	p.(Glu178Ala)
c.533A>G	c.A533G	E178G	p.(Glu178Gly)
c.532G>A	c.G532A	E178K	p.(Glu178Lys)
c.532G>C	c.G532C	E178Q	p.(Glu178Gln)
c.538T>A	c.T538A	L180M	p.(Leu180Met)
c.539T>C	c.T539C	L180S	p.(Leu180Ser)
c.541G>C	c.G541C	A181P	p.(Ala181Pro)
c.541G>A	c.G541A	A181T	p.(Ala181Thr)
c.542C>T	c.C542T	A181V	p.(Ala181Val)
c.545A>C	c.A545C	D182A	p.(Asp182Ala)
c.546T>A	c.T546A	D182E	p.(Asp182Glu)
c.545A>T	c.A545T	D182V	p.(Asp182Val)
c.544G>T	c.G544T	D182Y	p.(Asp182Tyr)
c.551A>T	c.A551T	Y184F	p.(Tyr184Phe)
c.550T>C	c.T550C	Y184H	p.(Tyr184His)
c.551A>C	c.A551C	Y184S	p.(Tyr184Ser)
c.554A>T	c.A554T	K185M	p.(Lys185Met)
c.555G>C	c.G555C	K185N	p.(Lys185Asn)
c.553A>C	c.A553C	K185Q	p.(Lys185Gln)
c.554A>C	c.A554C	K185T	p.(Lys185Thr)
c.556C>G	c.C556G	H186D	p.(His186Asp)
c.557A>T	c.A557T	H186L	p.(His186Leu)
c.556C>A	c.C556A	H186N	p.(His186Asn)
c.558C>G	c.C558G	H186Q	p.(His186Gln)
c.556C>T	c.C556T	H186Y	p.(His186Tyr)
c.559A>T	c.A559T	M187L	p.(Met187Leu)
c.562T>G	c.T562G	S188A	p.(Ser188Ala)
c.563C>G	c.C563G	S188C	p.(Ser188Cys)
c.563C>T	c.C563T	S188F	p.(Ser188Phe)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.562T>C	c.T562C	S188P	p.(Ser188Pro)
c.562T>A	c.T562A	S188T	p.(Ser188Thr)
c.563C>A	c.C563A	S188Y	p.(Ser188Tyr)
c.566T>C	c.T566C	L189S	p.(Leu189Ser)
c.565T>G	c.T565G	L189V	p.(Leu189Val)
c.569C>A	c.C569A	A190D	p.(Ala190Asp)
c.569C>G	c.C569G	A190G	p.(Ala190Gly)
c.568G>T	c.G568T	A190S	p.(Ala190Ser)
c.568G>A	c.G568A	A190T	p.(Ala190Thr)
c.569C>T	c.C569T	A190V	p.(Ala190Val)
c.571C>A	c.C571A	L191M	p.(Leu191Met)
c.571C>G	c.C571G	L191V	p.(Leu191Val)
c.574A>G	c.A574G	N192D	p.(Asn192Asp)
c.574A>C	c.A574C	N192H	p.(Asn192His)
c.576T>A	c.T576A	N192K	p.(Asn192Lys)
c.575A>G	c.A575G	N192S	p.(Asn192Ser)
c.575A>C	c.A575C	N192T	p.(Asn192Thr)
c.577A>G	c.A577G	R193G	p.(Arg193Gly)
c.578G>T	c.G578T	R193M	p.(Arg193Met)
c.578G>C	c.G578C	R193T	p.(Arg193Thr)
c.577A>T	c.A577T	R193W	p.(Arg193Trp)
c.581C>A	c.C581A	T194N	p.(Thr194Asn)
c.580A>C	c.A580C	T194P	p.(Thr194Pro)
c.580A>T	c.A580T	T194S	p.(Thr194Ser)
c.583G>T	c.G583T	G195C	p.(Gly195Cys)
c.583G>C	c.G583C	G195R	p.(Gly195Arg)
c.583G>A	c.G583A	G195S	p.(Gly195Ser)
c.587G>T	c.G587T	R196I	p.(Arg196Ile)
c.587G>A	c.G587A	R196K	p.(Arg196Lys)
c.589A>T	c.A589T	S197C	p.(Ser197Cys)
c.589A>G	c.A589G	S197G	p.(Ser197Gly)
c.590G>T	c.G590T	S197I	p.(Ser197Ile)
c.590G>A	c.G590A	S197N	p.(Ser197Asn)
c.590G>C	c.G590C	S197T	p.(Ser197Thr)
c.594T>G	c.T594G	I198M	p.(Ile198Met)
c.593T>G	c.T593G	I198S	p.(Ile198Ser)
c.596T>A	c.T596A	V199E	p.(Val199Glu)
c.595G>C	c.G595C	V199L	p.(Val199Leu)
c.598T>A	c.T598A	Y200N	p.(Tyr200Asn)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.599A>C	c.A599C	Y200S	p.(Tyr200Ser)
c.601T>G	c.T601G	S201A	p.(Ser201Ala)
c.602C>G	c.C602G	S201C	p.(Ser201Cys)
c.601T>A	c.T601A	S201T	p.(Ser201Thr)
c.608A>C	c.A608C	E203A	p.(Glu203Ala)
c.608A>G	c.A608G	E203G	p.(Glu203Gly)
c.607G>C	c.G607C	E203Q	p.(Glu203Gln)
c.611G>C	c.G611C	W204S	p.(Trp204Ser)
c.616C>T	c.C616T	L206F	p.(Leu206Phe)
c.617T>A	c.T617A	L206H	p.(Leu206His)
c.616C>A	c.C616A	L206I	p.(Leu206Ile)
c.617T>G	c.T617G	L206R	p.(Leu206Arg)
c.616C>G	c.C616G	L206V	p.(Leu206Val)
c.620A>T	c.A620T	Y207F	p.(Tyr207Phe)
c.623T>G	c.T623G	M208K	p.(Met208Lys)
c.627G>C	c.G627C	W209C	p.(Trp209Cys)
c.625T>G	c.T625G	W209G	p.(Trp209Gly)
c.629C>A	c.C629A	P210H	p.(Pro210His)
c.628C>A	c.C628A	P210T	p.(Pro210Thr)
c.632T>G	c.T632G	F211C	p.(Phe211Cys)
c.633T>A	c.T633A	F211L	p.(Phe211Leu)
c.632T>C	c.T632C	F211S	p.(Phe211Ser)
c.631T>G	c.T631G	F211V	p.(Phe211Val)
c.632T>A	c.T632A	F211Y	p.(Phe211Tyr)
c.636A>T	c.A636T	Q212H	p.(Gln212His)
c.635A>C	c.A635C	Q212P	p.(Gln212Pro)
c.637A>G	c.A637G	K213E	p.(Lys213Glu)
c.637A>C	c.A637C	K213Q	p.(Lys213Gln)
c.640C>G	c.C640G	P214A	p.(Pro214Ala)
c.641C>A	c.C641A	P214H	p.(Pro214His)
c.641C>G	c.C641G	P214R	p.(Pro214Arg)
c.640C>A	c.C640A	P214T	p.(Pro214Thr)
c.643A>C	c.A643C	N215H	p.(Asn215His)
c.645T>A	c.T645A	N215K	p.(Asn215Lys)
c.644A>C	c.A644C	N215T	p.(Asn215Thr)
c.643A>T	c.A643T	N215Y	p.(Asn215Tyr)
c.647A>T	c.A647T	Y216F	p.(Tyr216Phe)
c.646T>C	c.T646C	Y216H	p.(Tyr216His)
c.646T>A	c.T646A	Y216N	p.(Tyr216Asn)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.649A>G	c.A649G	T217A	p.(Thr217Ala)
c.650C>T	c.C650T	T217I	p.(Thr217Ile)
c.650C>A	c.C650A	T217K	p.(Thr217Lys)
c.649A>C	c.A649C	T217P	p.(Thr217Pro)
c.650C>G	c.C650G	T217R	p.(Thr217Arg)
c.649A>T	c.A649T	T217S	p.(Thr217Ser)
c.653A>C	c.A653C	E218A	p.(Glu218Ala)
c.654A>T	c.A654T	E218D	p.(Glu218Asp)
c.653A>G	c.A653G	E218G	p.(Glu218Gly)
c.652G>A	c.G652A	E218K	p.(Glu218Lys)
c.652G>C	c.G652C	E218Q	p.(Glu218Gln)
c.653A>T	c.A653T	E218V	p.(Glu218Val)
c.655A>T	c.A655T	I219F	p.(Ile219Phe)
c.657C>G	c.C657G	I219M	p.(Ile219Met)
c.656T>G	c.T656G	I219S	p.(Ile219Ser)
c.659G>T	c.G659T	R220L	p.(Arg220Leu)
c.661C>G	c.C661G	Q221E	p.(Gln221Glu)
c.663G>C	c.G663C	Q221H	p.(Gln221His)
c.661C>A	c.C661A	Q221K	p.(Gln221Lys)
c.662A>T	c.A662T	Q221L	p.(Gln221Leu)
c.662A>G	c.A662G	Q221R	p.(Gln221Arg)
c.665A>G	c.A665G	Y222C	p.(Tyr222Cys)
c.664T>G	c.T664G	Y222D	p.(Tyr222Asp)
c.664T>C	c.T664C	Y222H	p.(Tyr222His)
c.664T>A	c.T664A	Y222N	p.(Tyr222Asn)
c.665A>C	c.A665C	Y222S	p.(Tyr222Ser)
c.670A>C	c.A670C	N224H	p.(Asn224His)
c.679C>G	c.C679G	R227G	p.(Arg227Gly)
c.682A>C	c.A682C	N228H	p.(Asn228His)
c.683A>T	c.A683T	N228I	p.(Asn228Ile)
c.683A>C	c.A683C	N228T	p.(Asn228Thr)
c.685T>A	c.T685A	F229I	p.(Phe229Ile)
c.686T>C	c.T686C	F229S	p.(Phe229Ser)
c.686T>A	c.T686A	F229Y	p.(Phe229Tyr)
c.689C>A	c.C689A	A230D	p.(Ala230Asp)
c.689C>G	c.C689G	A230G	p.(Ala230Gly)
c.688G>C	c.G688C	A230P	p.(Ala230Pro)
c.689C>T	c.C689T	A230V	p.(Ala230Val)
c.694A>C	c.A694C	I232L	p.(Ile232Leu)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.696T>G	c.T696G	I232M	p.(Ile232Met)
c.694A>G	c.A694G	I232V	p.(Ile232Val)
c.698A>C	c.A698C	D233A	p.(Asp233Ala)
c.699T>A	c.T699A	D233E	p.(Asp233Glu)
c.698A>G	c.A698G	D233G	p.(Asp233Gly)
c.698A>T	c.A698T	D233V	p.(Asp233Val)
c.703T>G	c.T703G	S235A	p.(Ser235Ala)
c.703T>A	c.T703A	S235T	p.(Ser235Thr)
c.710A>T	c.A710T	K237I	p.(Lys237Ile)
c.712A>T	c.A712T	S238C	p.(Ser238Cys)
c.713G>T	c.G713T	S238I	p.(Ser238Ile)
c.713G>C	c.G713C	S238T	p.(Ser238Thr)
c.715A>T	c.A715T	I239L	p.(Ile239Leu)
c.718A>G	c.A718G	K240E	p.(Lys240Glu)
c.719A>T	c.A719T	K240M	p.(Lys240Met)
c.719A>G	c.A719G	K240R	p.(Lys240Arg)
c.721A>T	c.A721T	S241C	p.(Ser241Cys)
c.722G>T	c.G722T	S241I	p.(Ser241Ile)
c.722G>C	c.G722C	S241T	p.(Ser241Thr)
c.724A>C	c.A724C	I242L	p.(Ile242Leu)
c.726C>G	c.C726G	I242M	p.(Ile242Met)
c.725T>G	c.T725G	I242S	p.(Ile242Ser)
c.727T>A	c.T727A	L243M	p.(Leu243Met)
c.728T>C	c.T728C	L243S	p.(Leu243Ser)
c.727T>G	c.T727G	L243V	p.(Leu243Val)
c.731A>C	c.A731C	D244A	p.(Asp244Ala)
c.732C>G	c.C732G	D244E	p.(Asp244Glu)
c.731A>G	c.A731G	D244G	p.(Asp244Gly)
c.731A>T	c.A731T	D244V	p.(Asp244Val)
c.730G>T	c.G730T	D244Y	p.(Asp244Tyr)
c.735G>C	c.G735C	W245C	p.(Trp245Cys)
c.736A>G	c.A736G	T246A	p.(Thr246Ala)
c.737C>T	c.C737T	T246I	p.(Thr246Ile)
c.737C>A	c.C737A	T246K	p.(Thr246Lys)
c.737C>G	c.C737G	T246R	p.(Thr246Arg)
c.739T>G	c.T739G	S247A	p.(Ser247Ala)
c.740C>T	c.C740T	S247F	p.(Ser247Phe)
c.739T>A	c.T739A	S247T	p.(Ser247Thr)
c.740C>A	c.C740A	S247Y	p.(Ser247Tyr)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.743T>G	c.T743G	F248C	p.(Phe248Cys)
c.744T>A	c.T744A	F248L	p.(Phe248Leu)
c.742T>G	c.T742G	F248V	p.(Phe248Val)
c.743T>A	c.T743A	F248Y	p.(Phe248Tyr)
c.745A>G	c.A745G	N249D	p.(Asn249Asp)
c.745A>C	c.A745C	N249H	p.(Asn249His)
c.746A>T	c.A746T	N249I	p.(Asn249Ile)
c.746A>G	c.A746G	N249S	p.(Asn249Ser)
c.746A>C	c.A746C	N249T	p.(Asn249Thr)
c.745A>T	c.A745T	N249Y	p.(Asn249Tyr)
c.748C>G	c.C748G	Q250E	p.(Gln250Glu)
c.749A>T	c.A749T	Q250L	p.(Gln250Leu)
c.752A>G	c.A752G	E251G	p.(Glu251Gly)
c.751G>A	c.G751A	E251K	p.(Glu251Lys)
c.751G>C	c.G751C	E251Q	p.(Glu251Gln)
c.752A>T	c.A752T	E251V	p.(Glu251Val)
c.754A>G	c.A754G	R252G	p.(Arg252Gly)
c.757A>T	c.A757T	I253F	p.(Ile253Phe)
c.758T>A	c.T758A	I253N	p.(Ile253Asn)
c.757A>G	c.A757G	I253V	p.(Ile253Val)
c.761T>C	c.T761C	V254A	p.(Val254Ala)
c.761T>A	c.T761A	V254D	p.(Val254Asp)
c.760G>T	c.G760T	V254F	p.(Val254Phe)
c.761T>G	c.T761G	V254G	p.(Val254Gly)
c.764A>C	c.A764C	D255A	p.(Asp255Ala)
c.765T>A	c.T765A	D255E	p.(Asp255Glu)
c.763G>C	c.G763C	D255H	p.(Asp255His)
c.763G>A	c.G763A	D255N	p.(Asp255Asn)
c.764A>T	c.A764T	D255V	p.(Asp255Val)
c.763G>T	c.G763T	D255Y	p.(Asp255Tyr)
c.767T>A	c.T767A	V256D	p.(Val256Asp)
c.767T>G	c.T767G	V256G	p.(Val256Gly)
c.766G>C	c.G766C	V256L	p.(Val256Leu)
c.769G>T	c.G769T	A257S	p.(Ala257Ser)
c.773G>A	c.G773A	G258E	p.(Gly258Glu)
c.775C>G	c.C775G	P259A	p.(Pro259Ala)
c.775C>A	c.C775A	P259T	p.(Pro259Thr)
c.778G>T	c.G778T	G260W	p.(Gly260Trp)
c.782G>C	c.G782C	G261A	p.(Gly261Ala)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.787A>C	c.A787C	N263H	p.(Asn263His)
c.788A>C	c.A788C	N263T	p.(Asn263Thr)
c.790G>C	c.G790C	D264H	p.(Asp264His)
c.790G>A	c.G790A	D264N	p.(Asp264Asn)
c.793C>G	c.C793G	P265A	p.(Pro265Ala)
c.794C>A	c.C794A	P265Q	p.(Pro265Gln)
c.799A>T	c.A799T	M267L	p.(Met267Leu)
c.799A>G	c.A799G	M267V	p.(Met267Val)
c.804A>T	c.A804T	L268F	p.(Leu268Phe)
c.802T>A	c.T802A	L268I	p.(Leu268Ile)
c.805G>C	c.G805C	V269L	p.(Val269Leu)
c.808A>C	c.A808C	I270L	p.(Ile270Leu)
c.809T>G	c.T809G	I270S	p.(Ile270Ser)
c.808A>G	c.A808G	I270V	p.(Ile270Val)
c.814A>G	c.A814G	N272D	p.(Asn272Asp)
c.818T>A	c.T818A	F273Y	p.(Phe273Tyr)
c.823C>A	c.C823A	L275I	p.(Leu275Ile)
c.830G>T	c.G830T	W277L	p.(Trp277Leu)
c.833A>T	c.A833T	N278I	p.(Asn278Ile)
c.839A>T	c.A839T	Q280L	p.(Gln280Leu)
c.839A>G	c.A839G	Q280R	p.(Gln280Arg)
c.842T>C	c.T842C	V281A	p.(Val281Ala)
c.842T>A	c.T842A	V281E	p.(Val281Glu)
c.842T>G	c.T842G	V281G	p.(Val281Gly)
c.841G>C	c.G841C	V281L	p.(Val281Leu)
c.844A>T	c.A844T	T282S	p.(Thr282Ser)
c.847C>G	c.C847G	Q283E	p.(Gln283Glu)
c.849G>C	c.G849C	Q283H	p.(Gln283His)
c.848A>T	c.A848T	Q283L	p.(Gln283Leu)
c.852G>C	c.G852C	M284I	p.(Met284Ile)
c.850A>T	c.A850T	M284L	p.(Met284Leu)
c.854C>G	c.C854G	A285G	p.(Ala285Gly)
c.853G>A	c.G853A	A285T	p.(Ala285Thr)
c.854C>T	c.C854T	A285V	p.(Ala285Val)
c.856C>T	c.C856T	L286F	p.(Leu286Phe)
c.857T>A	c.T857A	L286H	p.(Leu286His)
c.856C>G	c.C856G	L286V	p.(Leu286Val)
c.863C>G	c.C863G	A288G	p.(Ala288Gly)
c.862G>T	c.G862T	A288S	p.(Ala288Ser)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.863C>T	c.C863T	A288V	p.(Ala288Val)
c.865A>C	c.A865C	I289L	p.(Ile289Leu)
c.866T>C	c.T866C	I289T	p.(Ile289Thr)
c.865A>G	c.A865G	I289V	p.(Ile289Val)
c.872C>G	c.C872G	A291G	p.(Ala291Gly)
c.875C>G	c.C875G	A292G	p.(Ala292Gly)
c.874G>T	c.G874T	A292S	p.(Ala292Ser)
c.882A>T	c.A882T	L294F	p.(Leu294Phe)
c.880T>A	c.T880A	L294I	p.(Leu294Ile)
c.880T>G	c.T880G	L294V	p.(Leu294Val)
c.883T>A	c.T883A	F295I	p.(Phe295Ile)
c.884T>C	c.T884C	F295S	p.(Phe295Ser)
c.883T>G	c.T883G	F295V	p.(Phe295Val)
c.884T>A	c.T884A	F295Y	p.(Phe295Tyr)
c.889T>A	c.T889A	S297T	p.(Ser297Thr)
c.892A>G	c.A892G	N298D	p.(Asn298Asp)
c.893A>T	c.A893T	N298I	p.(Asn298Ile)
c.893A>C	c.A893C	N298T	p.(Asn298Thr)
c.895G>C	c.G895C	D299H	p.(Asp299His)
c.895G>A	c.G895A	D299N	p.(Asp299Asn)
c.898C>A	c.C898A	L300I	p.(Leu300Ile)
c.898C>G	c.C898G	L300V	p.(Leu300Val)
c.904C>G	c.C904G	H302D	p.(His302Asp)
c.905A>T	c.A905T	H302L	p.(His302Leu)
c.904C>A	c.C904A	H302N	p.(His302Asn)
c.904C>T	c.C904T	H302Y	p.(His302Tyr)
c.908T>G	c.T908G	I303S	p.(Ile303Ser)
c.911G>T	c.G911T	S304I	p.(Ser304Ile)
c.916C>G	c.C916G	Q306E	p.(Gln306Glu)
c.917A>T	c.A917T	Q306L	p.(Gln306Leu)
c.917A>C	c.A917C	Q306P	p.(Gln306Pro)
c.920C>A	c.C920A	A307D	p.(Ala307Asp)
c.920C>G	c.C920G	A307G	p.(Ala307Gly)
c.919G>C	c.G919C	A307P	p.(Ala307Pro)
c.919G>T	c.G919T	A307S	p.(Ala307Ser)
c.920C>T	c.C920T	A307V	p.(Ala307Val)
c.923A>T	c.A923T	K308I	p.(Lys308Ile)
c.922A>C	c.A922C	K308Q	p.(Lys308Gln)
c.923A>G	c.A923G	K308R	p.(Lys308Arg)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.926C>A	c.C926A	A309D	p.(Ala309Asp)
c.925G>A	c.G925A	A309T	p.(Ala309Thr)
c.928C>A	c.C928A	L310I	p.(Leu310Ile)
c.931C>A	c.C931A	L311I	p.(Leu311Ile)
c.934C>G	c.C934G	Q312E	p.(Gln312Glu)
c.934C>A	c.C934A	Q312K	p.(Gln312Lys)
c.935A>T	c.A935T	Q312L	p.(Gln312Leu)
c.939T>A	c.T939A	D313E	p.(Asp313Glu)
c.938A>T	c.A938T	D313V	p.(Asp313Val)
c.940A>G	c.A940G	K314E	p.(Lys314Glu)
c.941A>T	c.A941T	K314M	p.(Lys314Met)
c.942G>C	c.G942C	K314N	p.(Lys314Asn)
c.941A>C	c.A941C	K314T	p.(Lys314Thr)
c.944A>C	c.A944C	D315A	p.(Asp315Ala)
c.944A>G	c.A944G	D315G	p.(Asp315Gly)
c.943G>C	c.G943C	D315H	p.(Asp315His)
c.943G>A	c.G943A	D315N	p.(Asp315Asn)
c.944A>T	c.A944T	D315V	p.(Asp315Val)
c.943G>T	c.G943T	D315Y	p.(Asp315Tyr)
c.947T>C	c.T947C	V316A	p.(Val316Ala)
c.946G>C	c.G946C	V316L	p.(Val316Leu)
c.949A>C	c.A949C	I317L	p.(Ile317Leu)
c.951T>G	c.T951G	I317M	p.(Ile317Met)
c.949A>G	c.A949G	I317V	p.(Ile317Val)
c.953C>A	c.C953A	A318D	p.(Ala318Asp)
c.952G>C	c.G952C	A318P	p.(Ala318Pro)
c.952G>A	c.G952A	A318T	p.(Ala318Thr)
c.953C>T	c.C953T	A318V	p.(Ala318Val)
c.957C>G	c.C957G	I319M	p.(Ile319Met)
c.959A>G	c.A959G	N320S	p.(Asn320Ser)
c.959A>C	c.A959C	N320T	p.(Asn320Thr)
c.961C>A	c.C961A	Q321K	p.(Gln321Lys)
c.965A>C	c.A965C	D322A	p.(Asp322Ala)
c.965A>T	c.A965T	D322V	p.(Asp322Val)
c.970T>G	c.T970G	L324V	p.(Leu324Val)
c.971T>G	c.T971G	L324W	p.(Leu324Trp)
c.974G>C	c.G974C	G325A	p.(Gly325Ala)
c.973G>T	c.G973T	G325C	p.(Gly325Cys)
c.974G>T	c.G974T	G325V	p.(Gly325Val)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.976A>G	c.A976G	K326E	p.(Lys326Glu)
c.977A>T	c.A977T	K326M	p.(Lys326Met)
c.976A>C	c.A976C	K326Q	p.(Lys326Gln)
c.977A>G	c.A977G	K326R	p.(Lys326Arg)
c.977A>C	c.A977C	K326T	p.(Lys326Thr)
c.981A>T	c.A981T	Q327H	p.(Gln327His)
c.980A>C	c.A980C	Q327P	p.(Gln327Pro)
c.986A>G	c.A986G	Y329C	p.(Tyr329Cys)
c.985T>G	c.T985G	Y329D	p.(Tyr329Asp)
c.986A>T	c.A986T	Y329F	p.(Tyr329Phe)
c.985T>C	c.T985C	Y329H	p.(Tyr329His)
c.985T>A	c.T985A	Y329N	p.(Tyr329Asn)
c.988C>G	c.C988G	Q330E	p.(Gln330Glu)
c.990G>C	c.G990C	Q330H	p.(Gln330His)
c.988C>A	c.C988A	Q330K	p.(Gln330Lys)
c.992T>A	c.T992A	L331H	p.(Leu331His)
c.992T>C	c.T992C	L331P	p.(Leu331Pro)
c.992T>G	c.T992G	L331R	p.(Leu331Arg)
c.991C>G	c.C991G	L331V	p.(Leu331Val)
c.994A>G	c.A994G	R332G	p.(Arg332Gly)
c.995G>T	c.G995T	R332I	p.(Arg332Ile)
c.996A>T	c.A996T	R332S	p.(Arg332Ser)
c.995G>C	c.G995C	R332T	p.(Arg332Thr)
c.997C>G	c.C997G	Q333E	p.(Gln333Glu)
c.998A>T	c.A998T	Q333L	p.(Gln333Leu)
c.998A>C	c.A998C	Q333P	p.(Gln333Pro)
c.1000G>C	c.G1000C	G334R	p.(Gly334Arg)
c.1001G>T	c.G1001T	G334V	p.(Gly334Val)
c.1004A>C	c.A1004C	D335A	p.(Asp335Ala)
c.1005C>G	c.C1005G	D335E	p.(Asp335Glu)
c.1004A>G	c.A1004G	D335G	p.(Asp335Gly)
c.1004A>T	c.A1004T	D335V	p.(Asp335Val)
c.1003G>T	c.G1003T	D335Y	p.(Asp335Tyr)
c.1006A>G	c.A1006G	N336D	p.(Asn336Asp)
c.1007A>T	c.A1007T	N336I	p.(Asn336Ile)
c.1007A>G	c.A1007G	N336S	p.(Asn336Ser)
c.1007A>C	c.A1007C	N336T	p.(Asn336Thr)
c.1006A>T	c.A1006T	N336Y	p.(Asn336Tyr)
c.1010T>G	c.T1010G	F337C	p.(Phe337Cys)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1011T>A	c.T1011A	F337L	p.(Phe337Leu)
c.1009T>G	c.T1009G	F337V	p.(Phe337Val)
c.1010T>A	c.T1010A	F337Y	p.(Phe337Tyr)
c.1013A>C	c.A1013C	E338A	p.(Glu338Ala)
c.1014A>T	c.A1014T	E338D	p.(Glu338Asp)
c.1013A>G	c.A1013G	E338G	p.(Glu338Gly)
c.1015G>A	c.G1015A	V339M	p.(Val339Met)
c.1022A>C	c.A1022C	E341A	p.(Glu341Ala)
c.1021G>C	c.G1021C	E341Q	p.(Glu341Gln)
c.1027C>G	c.C1027G	P343A	p.(Pro343Ala)
c.1027C>T	c.C1027T	P343S	p.(Pro343Ser)
c.1030C>T	c.C1030T	L344F	p.(Leu344Phe)
c.1031T>G	c.T1031G	L344R	p.(Leu344Arg)
c.1030C>G	c.C1030G	L344V	p.(Leu344Val)
c.1037G>C	c.G1037C	G346A	p.(Gly346Ala)
c.1036G>T	c.G1036T	G346C	p.(Gly346Cys)
c.1037G>A	c.G1037A	G346D	p.(Gly346Asp)
c.1037G>T	c.G1037T	G346V	p.(Gly346Val)
c.1039T>A	c.T1039A	L347I	p.(Leu347Ile)
c.1043C>A	c.C1043A	A348D	p.(Ala348Asp)
c.1047G>C	c.G1047C	W349C	p.(Trp349Cys)
c.1046G>T	c.G1046T	W349L	p.(Trp349Leu)
c.1049C>G	c.C1049G	A350G	p.(Ala350Gly)
c.1048G>T	c.G1048T	A350S	p.(Ala350Ser)
c.1048G>A	c.G1048A	A350T	p.(Ala350Thr)
c.1049C>T	c.C1049T	A350V	p.(Ala350Val)
c.1052T>C	c.T1052C	V351A	p.(Val351Ala)
c.1052T>A	c.T1052A	V351E	p.(Val351Glu)
c.1054G>T	c.G1054T	A352S	p.(Ala352Ser)
c.1054G>A	c.G1054A	A352T	p.(Ala352Thr)
c.1058T>A	c.T1058A	M353K	p.(Met353Lys)
c.1057A>T	c.A1057T	M353L	p.(Met353Leu)
c.1058T>C	c.T1058C	M353T	p.(Met353Thr)
c.1061T>G	c.T1061G	I354R	p.(Ile354Arg)
c.1063A>G	c.A1063G	N355D	p.(Asn355Asp)
c.1063A>C	c.A1063C	N355H	p.(Asn355His)
c.1064A>G	c.A1064G	N355S	p.(Asn355Ser)
c.1063A>T	c.A1063T	N355Y	p.(Asn355Tyr)
c.1067G>T	c.G1067T	R356L	p.(Arg356Leu)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1069C>G	c.C1069G	Q357E	p.(Gln357Glu)
c.1075A>T	c.A1075T	I359F	p.(Ile359Phe)
c.1075A>C	c.A1075C	I359L	p.(Ile359Leu)
c.1076T>A	c.T1076A	I359N	p.(Ile359Asn)
c.1076T>G	c.T1076G	I359S	p.(Ile359Ser)
c.1075A>G	c.A1075G	I359V	p.(Ile359Val)
c.1084C>G	c.C1084G	P362A	p.(Pro362Ala)
c.1085C>A	c.C1085A	P362H	p.(Pro362His)
c.1085C>G	c.C1085G	P362R	p.(Pro362Arg)
c.1084C>T	c.C1084T	P362S	p.(Pro362Ser)
c.1087C>G	c.C1087G	R363G	p.(Arg363Gly)
c.1088G>T	c.G1088T	R363L	p.(Arg363Leu)
c.1087C>A	c.C1087A	R363S	p.(Arg363Ser)
c.1091C>G	c.C1091G	S364C	p.(Ser364Cys)
c.1090T>C	c.T1090C	S364P	p.(Ser364Pro)
c.1093T>G	c.T1093G	Y365D	p.(Tyr365Asp)
c.1094A>T	c.A1094T	Y365F	p.(Tyr365Phe)
c.1093T>A	c.T1093A	Y365N	p.(Tyr365Asn)
c.1094A>C	c.A1094C	Y365S	p.(Tyr365Ser)
c.1097C>T	c.C1097T	T366I	p.(Thr366Ile)
c.1097C>A	c.C1097A	T366N	p.(Thr366Asn)
c.1096A>C	c.A1096C	T366P	p.(Thr366Pro)
c.1096A>T	c.A1096T	T366S	p.(Thr366Ser)
c.1099A>T	c.A1099T	I367F	p.(Ile367Phe)
c.1099A>C	c.A1099C	I367L	p.(Ile367Leu)
c.1101C>G	c.C1101G	I367M	p.(Ile367Met)
c.1103C>G	c.C1103G	A368G	p.(Ala368Gly)
c.1102G>C	c.G1102C	A368P	p.(Ala368Pro)
c.1106T>C	c.T1106C	V369A	p.(Val369Ala)
c.1105G>T	c.G1105T	V369F	p.(Val369Phe)
c.1106T>G	c.T1106G	V369G	p.(Val369Gly)
c.1105G>A	c.G1105A	V369I	p.(Val369Ile)
c.1105G>C	c.G1105C	V369L	p.(Val369Leu)
c.1109C>A	c.C1109A	A370D	p.(Ala370Asp)
c.1109C>G	c.C1109G	A370G	p.(Ala370Gly)
c.1108G>C	c.G1108C	A370P	p.(Ala370Pro)
c.1108G>A	c.G1108A	A370T	p.(Ala370Thr)
c.1109C>T	c.C1109T	A370V	p.(Ala370Val)
c.1112C>G	c.C1112G	S371C	p.(Ser371Cys)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1111T>A	c.T1111A	S371T	p.(Ser371Thr)
c.1118G>C	c.G1118C	G373A	p.(Gly373Ala)
c.1117G>T	c.G1117T	G373C	p.(Gly373Cys)
c.1120A>G	c.A1120G	K374E	p.(Lys374Glu)
c.1121A>T	c.A1121T	K374I	p.(Lys374Ile)
c.1121A>G	c.A1121G	K374R	p.(Lys374Arg)
c.1121A>C	c.A1121C	K374T	p.(Lys374Thr)
c.1123G>C	c.G1123C	G375R	p.(Gly375Arg)
c.1127T>A	c.T1127A	V376E	p.(Val376Glu)
c.1127T>G	c.T1127G	V376G	p.(Val376Gly)
c.1126G>C	c.G1126C	V376L	p.(Val376Leu)
c.1126G>A	c.G1126A	V376M	p.(Val376Met)
c.1130C>G	c.C1130G	A377G	p.(Ala377Gly)
c.1129G>C	c.G1129C	A377P	p.(Ala377Pro)
c.1129G>T	c.G1129T	A377S	p.(Ala377Ser)
c.1129G>A	c.G1129A	A377T	p.(Ala377Thr)
c.1135A>G	c.A1135G	N379D	p.(Asn379Asp)
c.1136A>T	c.A1136T	N379I	p.(Asn379Ile)
c.1137T>A	c.T1137A	N379K	p.(Asn379Lys)
c.1136A>C	c.A1136C	N379T	p.(Asn379Thr)
c.1138C>G	c.C1138G	P380A	p.(Pro380Ala)
c.1139C>A	c.C1139A	P380H	p.(Pro380His)
c.1139C>G	c.C1139G	P380R	p.(Pro380Arg)
c.1138C>A	c.C1138A	P380T	p.(Pro380Thr)
c.1142C>A	c.C1142A	A381D	p.(Ala381Asp)
c.1148T>G	c.T1148G	F383C	p.(Phe383Cys)
c.1147T>A	c.T1147A	F383I	p.(Phe383Ile)
c.1148T>A	c.T1148A	F383Y	p.(Phe383Tyr)
c.1150A>T	c.A1150T	I384F	p.(Ile384Phe)
c.1152C>G	c.C1152G	I384M	p.(Ile384Met)
c.1151T>C	c.T1151C	I384T	p.(Ile384Thr)
c.1154C>T	c.C1154T	T385I	p.(Thr385Ile)
c.1158G>C	c.G1158C	Q386H	p.(Gln386His)
c.1156C>A	c.C1156A	Q386K	p.(Gln386Lys)
c.1157A>T	c.A1157T	Q386L	p.(Gln386Leu)
c.1159C>T	c.C1159T	L387F	p.(Leu387Phe)
c.1160T>A	c.T1160A	L387H	p.(Leu387His)
c.1159C>A	c.C1159A	L387I	p.(Leu387Ile)
c.1160T>G	c.T1160G	L387R	p.(Leu387Arg)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1162C>T	c.C1162T	L388F	p.(Leu388Phe)
c.1163T>A	c.T1163A	L388H	p.(Leu388His)
c.1162C>A	c.C1162A	L388I	p.(Leu388Ile)
c.1163T>G	c.T1163G	L388R	p.(Leu388Arg)
c.1162C>G	c.C1162G	L388V	p.(Leu388Val)
c.1172A>T	c.A1172T	K391I	p.(Lys391Ile)
c.1173A>T	c.A1173T	K391N	p.(Lys391Asn)
c.1171A>C	c.A1171C	K391Q	p.(Lys391Gln)
c.1172A>G	c.A1172G	K391R	p.(Lys391Arg)
c.1174A>G	c.A1174G	R392G	p.(Arg392Gly)
c.1175G>A	c.G1175A	R392K	p.(Arg392Lys)
c.1175G>T	c.G1175T	R392M	p.(Arg392Met)
c.1174A>T	c.A1174T	R392W	p.(Arg392Trp)
c.1177A>G	c.A1177G	K393E	p.(Lys393Glu)
c.1179G>C	c.G1179C	K393N	p.(Lys393Asn)
c.1177A>C	c.A1177C	K393Q	p.(Lys393Gln)
c.1178A>C	c.A1178C	K393T	p.(Lys393Thr)
c.1180C>A	c.C1180A	L394I	p.(Leu394Ile)
c.1181T>A	c.T1181A	L394Q	p.(Leu394Gln)
c.1181T>G	c.T1181G	L394R	p.(Leu394Arg)
c.1183G>C	c.G1183C	G395R	p.(Gly395Arg)
c.1187T>G	c.T1187G	F396C	p.(Phe396Cys)
c.1186T>A	c.T1186A	F396I	p.(Phe396Ile)
c.1188C>G	c.C1188G	F396L	p.(Phe396Leu)
c.1186T>G	c.T1186G	F396V	p.(Phe396Val)
c.1190A>G	c.A1190G	Y397C	p.(Tyr397Cys)
c.1190A>T	c.A1190T	Y397F	p.(Tyr397Phe)
c.1189T>C	c.T1189C	Y397H	p.(Tyr397His)
c.1189T>A	c.T1189A	Y397N	p.(Tyr397Asn)
c.1190A>C	c.A1190C	Y397S	p.(Tyr397Ser)
c.1193A>G	c.A1193G	E398G	p.(Glu398Gly)
c.1192G>C	c.G1192C	E398Q	p.(Glu398Gln)
c.1195T>G	c.T1195G	W399G	p.(Trp399Gly)
c.1195T>A	c.T1195A	W399R	p.(Trp399Arg)
c.1198A>G	c.A1198G	T400A	p.(Thr400Ala)
c.1199C>T	c.C1199T	T400I	p.(Thr400Ile)
c.1199C>A	c.C1199A	T400N	p.(Thr400Asn)
c.1198A>C	c.A1198C	T400P	p.(Thr400Pro)
c.1198A>T	c.A1198T	T400S	p.(Thr400Ser)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1201T>G	c.T1201G	S401A	p.(Ser401Ala)
c.1202C>T	c.C1202T	S401L	p.(Ser401Leu)
c.1201T>A	c.T1201A	S401T	p.(Ser401Thr)
c.1204A>G	c.A1204G	R402G	p.(Arg402Gly)
c.1205G>T	c.G1205T	R402M	p.(Arg402Met)
c.1206G>C	c.G1206C	R402S	p.(Arg402Ser)
c.1205G>C	c.G1205C	R402T	p.(Arg402Thr)
c.1204A>T	c.A1204T	R402W	p.(Arg402Trp)
c.1209A>T	c.A1209T	L403F	p.(Leu403Phe)
c.1207T>G	c.T1207G	L403V	p.(Leu403Val)
c.1210A>G	c.A1210G	R404G	p.(Arg404Gly)
c.1211G>T	c.G1211T	R404I	p.(Arg404Ile)
c.1211G>A	c.G1211A	R404K	p.(Arg404Lys)
c.1212A>T	c.A1212T	R404S	p.(Arg404Ser)
c.1211G>C	c.G1211C	R404T	p.(Arg404Thr)
c.1213A>G	c.A1213G	S405G	p.(Ser405Gly)
c.1216C>G	c.C1216G	H406D	p.(His406Asp)
c.1217A>T	c.A1217T	H406L	p.(His406Leu)
c.1218C>G	c.C1218G	H406Q	p.(His406Gln)
c.1219A>T	c.A1219T	I407L	p.(Ile407Leu)
c.1221A>G	c.A1221G	I407M	p.(Ile407Met)
c.1220T>C	c.T1220C	I407T	p.(Ile407Thr)
c.1222A>G	c.A1222G	N408D	p.(Asn408Asp)
c.1222A>C	c.A1222C	N408H	p.(Asn408His)
c.1223A>C	c.A1223C	N408T	p.(Asn408Thr)
c.1226C>T	c.C1226T	P409L	p.(Pro409Leu)
c.1228A>T	c.A1228T	T410S	p.(Thr410Ser)
c.1232G>C	c.G1232C	G411A	p.(Gly411Ala)
c.1231G>T	c.G1231T	G411C	p.(Gly411Cys)
c.1232G>T	c.G1232T	G411V	p.(Gly411Val)
c.1234A>G	c.A1234G	T412A	p.(Thr412Ala)
c.1235C>T	c.C1235T	T412I	p.(Thr412Ile)
c.1234A>T	c.A1234T	T412S	p.(Thr412Ser)
c.1237G>T	c.G1237T	V413F	p.(Val413Phe)
c.1238T>G	c.T1238G	V413G	p.(Val413Gly)
c.1237G>A	c.G1237A	V413I	p.(Val413Ile)
c.1242G>C	c.G1242C	L414F	p.(Leu414Phe)
c.1240T>G	c.T1240G	L414V	p.(Leu414Val)
c.1244T>A	c.T1244A	L415H	p.(Leu415His)

Table 2

Nucleotide change	Nucleotide change	Protein change (1 Letter)	Protein Change (3 Letter)
c.1243C>A	c.C1243A	L415I	p.(Leu415Ile)
c.1246C>G	c.C1246G	Q416E	p.(Gln416Glu)
c.1248G>C	c.G1248C	Q416H	p.(Gln416His)
c.1247A>T	c.A1247T	Q416L	p.(Gln416Leu)
c.1249C>A	c.C1249A	L417I	p.(Leu417Ile)
c.1253A>C	c.A1253C	E418A	p.(Glu418Ala)
c.1254A>T	c.A1254T	E418D	p.(Glu418Asp)
c.1252G>A	c.G1252A	E418K	p.(Glu418Lys)
c.1252G>C	c.G1252C	E418Q	p.(Glu418Gln)
c.1256A>T	c.A1256T	N419I	p.(Asn419Ile)
c.1256A>G	c.A1256G	N419S	p.(Asn419Ser)
c.1256A>C	c.A1256C	N419T	p.(Asn419Thr)
c.1255A>T	c.A1255T	N419Y	p.(Asn419Tyr)
c.1259C>A	c.C1259A	T420K	p.(Thr420Lys)
c.1258A>C	c.A1258C	T420P	p.(Thr420Pro)
c.1259C>G	c.C1259G	T420R	p.(Thr420Arg)
c.1258A>T	c.A1258T	T420S	p.(Thr420Ser)
c.1263G>C	c.G1263C	M421I	p.(Met421Ile)
c.1262T>A	c.T1262A	M421K	p.(Met421Lys)
c.1261A>T	c.A1261T	M421L	p.(Met421Leu)
c.1262T>G	c.T1262G	M421R	p.(Met421Arg)
c.1262T>C	c.T1262C	M421T	p.(Met421Thr)
c.1265A>C	c.A1265C	Q422P	p.(Gln422Pro)
c.1269G>C	c.G1269C	M423I	p.(Met423Ile)
c.1268T>A	c.T1268A	M423K	p.(Met423Lys)
c.1267A>T	c.A1267T	M423L	p.(Met423Leu)
c.1268T>C	c.T1268C	M423T	p.(Met423Thr)
c.1271C>T	c.C1271T	S424L	p.(Ser424Leu)
c.1275A>T	c.A1275T	L425F	p.(Leu425Phe)
c.1279G>A	c.G1279A	D427N	p.(Asp427Asn)
c.1286T>G	c.T1286G	L429R	p.(Leu429Arg)

[0096] Accordingly, in various embodiments, migalastat is used to treat Fabry disease and/or enhance α-Gal A activity in a patient having a GLA mutation selected from the group consisting of the nucleotide changes presented in Table 2. In various embodiments, these GLA mutations are relative to the nucleic sequence shown in SEQ ID NO: 3.

[0097] Further prophetic amenable mutations identified include V22G, A29D, D33H, N34H, G35A, R38S, N53K, N53Y, Q57R, F69L, G80V, Y88C, Y88S, M96V, Q107R, R112L, V124G, H125Y, I133M, I133F, A143V, Y152D, Y152N, D155E, A156S, Q157H, F159C, A160D, D165N, F169I, G171S, L180V, D182G, L189F, T194A, R196T, W204L, W204G, W209R, N215I, Y216S, I219L, N224T, N228D, S238G, I239M, K240N, Q250K, A257V, A257T, P259Q, P259S, G271A, L275V, S276T, N278Y, M290V, M290T, A291S, I303T, I303V, K308E, L310V, N320H, D322H, P323T, Q330P, F337S, E338V, V339A, P343T, E358Q, G360A, G360R, G375A, P380L, K391E, R392T, L394P, N408Y, G411S, T412P, and N419D. These mutations are also presented in Table 3 with their corresponding nucleotide changes.

[0098] Accordingly, in one or more embodiments, migalastat is used to treat Fabry disease and/or enhance α-Gal A activity in a patient having an α-Gal A mutation selected from the group consisting of the mutations presented in Table 3. In various embodiments, these α-Gal A mutations are relative to the amino acid sequence shown in SEQ ID NO: 2.

[0099] Exemplary nucleotide changes associated with these novel mutations are shown in Table 3 below:

Table 3

Nucleotide change	Protein change (1 Letter)
c.65T>G	V22G
c.86C>A	A29D
c.97G>C	D33H
c.100A>C	N34H
c.104G>C	G35A
c.114G>C	R38S
c.159C>G or c.159C>A	N53K
c.157A>T	N53Y
c.170A>G	Q57R
c.207C>A or c.207C>G	F69L
c.239G>T	G80V
c.263A>G	Y88C
c.263A>C	Y88S
c.286A>G	M96V
c.320A>G	Q107R
c.335G>T	R112L
c.371T>G	V124G
c.373C>T	H125Y

Table 3

Nucleotide change	Protein change (1 Letter)
c.399T>G	I133M
c.397A>T	I133F
c.428C>T	A143V
c.454T>G	Y152D
c.454T>A	Y152N
c.465T>A or c.465T>G	D155E
c.466G>T	A156S
c.471G>C or c.471G>T	Q157H
c.476T>G	F159C
c.479C>A	A160D
c.493G>A	D165N
c.505T>A	F169I
c.511G>A	G171S
c.538T>G	L180V
c.545A>G	D182G
c.567G>C or c.567G>T	L189F
c.580A>G	T194A
c.587G>C	R196T
c.611G>T	W204L
c.610T>G	W204G
c.625T>A	W209R
c.644A>T	N215I
c.647A>C	Y216S
c.655A>C	I219L
c.671A>C	N224T
c.682A>G	N228D
c.712A>G	S238G
c.717A>G	I239M
c.720G>C or c.720G>T	K240N
c.748C>A	Q250K
c.770C>T	A257V
c.769G>A	A257T
c.776C>A	P259Q
c.775C>T	P259S
c.812G>C	G271A
c.823C>G	L275V
c.827G>C	S276T
c.832A>T	N278Y
c.868A>G	M290V

Table 3

Nucleotide change	Protein change (1 Letter)
c.869T>C	M290T
c.871G>T	A291S
c.908T>C	I303T
c.907A>G	I303V
c.922A>G	K308E
c.928C>G	L310V
c.958A>C	N320H
c.964G>C	D322H
c.967C>A	P323T
c.989A>C	Q330P
c.1010T>C	F337S
c.1013A>T	E338V
c.1016T>C	V339A
c.1027C>A	P343T
c.1072G>C	E358Q
c.1079G>C	G360A
c.1078G>C	G360R
c.1124G>C	G375A
c.1139C>T	P380L
c.1171A>G	K391E
c.1175G>C	R392T
c.1181T>C	L394P
c.1222A>T	N408Y
c.1231G>A	G411S
c.1234A>C	T412P
c.1255A>G	N419D

[00100] Accordingly, in various embodiments, migalastat is used to treat Fabry disease and/or enhance α-Gal A activity in a patient having a GLA mutation selected from the group consisting of the nucleotide changes presented in Table 3. In various embodiments, these GLA mutations are relative to the nucleic sequence shown in SEQ ID NO: 3.

[00101] While the amenable mutations presented in Table 2 and Table 3 were initially prophetic amenable mutations evaluated by HEK assay, later-identified patients have since presented with several of these mutations. Accordingly, the mutations listed in Table 4 are now patient-associated amenable mutations, thus confirming that the prophetic mutations

described herein may later present in patients and that such patients can be treated with migalastat.

Table 4

Nucleotide change	Protein change (1 Letter)
c.23T>A	L8Q
c.65T>G	V22G
c.86C>A	A29D
c.97G>C	D33H
c.100A>C	N34H
c.104G>C	G35A
c.114G>C	R38S
c.159C>G or c.159C>A	N53K
c.157A>T	N53Y
c.170A>G	Q57R
c.207C>A or c.207C>G	F69L
c.239G>T	G80V
c.263A>G	Y88C
c.263A>C	Y88S
c.286A>G	M96V
c.320A>G	Q107R
c.335G>T	R112L
c.371T>G	V124G
c.373C>T	H125Y
c.399T>G	I133M
c.397A>T	I133F
c.428C>T	A143V
c.454T>G	Y152D
c.454T>A	Y152N
c.455A>C	Y152S
c.465T>A or c.465T>G	D155E
c.466G>T	A156S
c.471G>C or c.471G>T	Q157H
c.476T>G	F159C
c.479C>A	A160D
c.493G>A	D165N
c.505T>A	F169I
c.511G>A	G171S
c.538T>G	L180V
c.545A>G	D182G
c.551A>C	Y184S
c.567G>C or c.567G>T	L189F

Table 4

Nucleotide change	Protein change (1 Letter)
c.580A>G	T194A
c.587G>C	R196T
c.598T>A	Y200N
c.611G>T	W204L
c.610T>G	W204G
c.625T>A	W209R
c.644A>T	N215I
c.647A>C	Y216S
c.655A>C	I219L
c.664T>G	Y222D
c.671A>C	N224T
c.682A>G	N228D
c.712A>G	S238G
c.717A>G	I239M
c.720G>C or c.720G>T	K240N
c.748C>A	Q250K
c.770C>T	A257V
c.769G>A	A257T
c.776C>A	P259Q
c.775C>T	P259S
c.812G>C	G271A
c.823C>G	L275V
c.827G>C	S276T
c.832A>T	N278Y
c.868A>G	M290V
c.869T>C	M290T
c.871G>T	A291S
c.908T>C	I303T
c.907A>G	I303V
c.922A>G	K308E
c.928C>G	L310V
c.958A>C	N320H
c.964G>C	D322H
c.967C>A	P323T
c.973G>T	G325C
c.989A>C	Q330P
c.1010T>C	F337S
c.1013A>T	E338V
c.1016T>C	V339A

Table 4

Nucleotide change	Protein change (1 Letter)
c.1027C>A	P343T
c.1072G>C	E358Q
c.1079G>C	G360A
c.1078G>C	G360R
c.1093T>A	Y365N
c.1124G>C	G375A
c.1139C>T	P380L
c.1162C>T	L388F
c.1171A>G	K391E
c.1175G>C	R392T
c.1181T>C	L394P
c.1181T>G	L394R
c.1222A>T	N408Y
c.1231G>A	G411S
c.1234A>C	T412P
c.1255A>G	N419D

[00102] In addition to the prophetic amenable mutations identified above in Tables 2 and 3, several new mutations have been identified and determined to be mutations that are not amenable to migalastat therapy.

[00103] As described above, those mutations which were not found to be HEK assay amenable were labelled as prophetic non-amenable mutations. When multiple different nucleotide changes within a single codon lead to the same amino acid residue substitution on that position, the protein sequence change was listed as a single entry with alternative nucleotide changes.

[00104] The prophetic non-amenable mutations identified include Q2E, Q2K, Q2L, Q2P, Q2R, Q2H, L3M, L3Q, L3R, R4G, R4W, R4K, R4T, R4M, R4S, N5I, N5Y, N5H, N5T, N5S, P6A, E7Q, E7A, E7G, L8R, L8V, H9D, H9P, H9N, G11A, C12F, C12W, A13S, A13V, L14R, L14I, A15V, A15S, L16R, L16I, L16F, R17L, F18V, F18Y, L19M, L19V, L19R, A20S, A20T, L21I, L21V, V22D, S23A, S23C, S23Y, S23F, W24L, D25G, D25Y, D25A, D25E, D25V, D25N, I26F, I26L, I26M, I26S, I26T, I26V, P27H, P27R, G28A, G28V, A29S, A29T, R30I, R30K, R30S, R30T, A31T, A31E, A31G, A31P, A31S, D33N, N34I, N34Y, R38K, R38T, T39P, P40T, T41P, G43C, W44G, W44L, W44R, W44S, L45Q, W47S, E48G, E48V, R49H, F50I, F50L, F50S, F50V, M51L, C52F, L54I, D55N, C56R, Q57E, Q57H,

Q57K, Q57P, E58A, E58G, E58Q, E58D, E58V, D61A, D61G, D61H, D61N, D61Y, S62T, C63F, C63G, C63W, I64F, I64M, I64N, I64S, I64T, E66A, K67R, L68V, L68H, L68P, L68R, F69V, F69C, F69S, M70V, M70T, E71K, M72K, A73P, A73G, E74Q, E74A, L75V, L75H, L75I, L75R, M76K, M76L, M76I, V77F, V77A, V77G, V77D, S78T, S78A, G80R, W81G, K82Q, D83Y, D83H, G85V, Y86N, Y86S, E87K, E87A, E87V, E87Q, Y88F, L89I, C90F, C90G, C90S, I91V, I91N, D92A, D92E, D93A, D93H, C94R, C94W, W95R, M96K, M96R, A97G, P98A, P98S, P98T, Q99H, Q99K, R100G, R100I, R100S, D101N, D101Y, E103A, E103D, E103G, E103K, E103V, G104C, G104R, R105S, Q107P, A108G, A108P, A108S, D109V, P110H, P110S, Q111E, Q111H, Q111R, Q111K, Q111L, Q111P, R112P, F113C, P114A, P114H, P114S, P114T, P114R, H115L, H115P, H115Q, H115R, H115Y, G116W, G116A, G116E, I117F, I117L, I117N, I117V, R118G, R118P, R118S, R118L, R118H, Q119E, Q119H, Q119K, Q119L, Q119P, L120I, L120Q, L120R, A121S, A121D, A121G, N122D, N122H, N122I, N122K, N122S, N122T, N122Y, Y123H, V124L, V124A, V124F, H125Q, S126T, S126R, S126N, K127Q, K127T, K127R, K127I, K127N, G128R, G128V, L129M, L129Q, L129R, K130E, K130T, L131Q, L131I, L131R, G132W, G132V, I133S, Y134N, Y134C, Y134F, A135P, D136G, V137F, G138V, N139D, T141P, T141A, C142S, C142G, C142F, A143S, F145I, G147W, G147V, S148I, F149I, F149V, F149Y, F149L, F149S, G150A, G150R, Y151H, Y151N, Y151F, D153E, D153G, I154F, I154L, I154M, I154N, I154S, I154T, I154V, D155A, D155G, D155N, D155V, D155Y, A156P, Q157R, T158P, F159S, A160P, D161A, D161E, D161G, G163A, G163E, G163R, V164E, L166P, L166R, L167R, K168Q, K168E, K168I, K168T, D170A, D170E, D170Y, Y173D, Y173N, C174F, C174S, C174W, C174Y, D175A, S176G, S176I, S176N, S176T, E178D, E178V, N179D, N179H, N179I, N179K, N179S, N179T, N179Y, A181S, A181E, A181G, D182N, D182H, Y184D, K185R, H186R, M187K, L189M, L189W, A190P, L191R, N192Y, N192I, R193K, R193S, G195A, G195D, S197R, I198F, I198L, I198N, I198V, Y200D, Y200F, Y200H, C202F, C202G, C202S, P205A, P205H, Y207D, Y207N, M208I, M208L, M208T, M208V, W209L, W209S, P210A, P210R, F211I, Q212E, Q212K, Q212L, Q212R, K213T, I219V, R220G, Y222F, C223S, C223F, C223W, N224K, N224Y, N224I, H225N, H225Y, H225P, H225L, H225Q, W226G, W226S, W226L, R227L, N228Y, N228K, F229V, F229C, A230S, D231H, D231Y, D231A, D231E, I232N, I232F, D233N, D233H, D233Y, D234N, D234H, D234A, D234G, S235P, W236G, W236S, K237E, K237N, K237Q, K237R, K237T, I239K, I239R, I239V, K240Q, K240T, S241G, S241N, S241R, W245R, W245S, T246P,

T246S, F248I, F248S, E251A, E251D, R252I, R252K, R252S, I253M, I253L, V254I, V254L, D255G, V256F, V256I, V256A, G258A, G260R, G260V, W262R, W262G, W262S, N263D, N263I, N263K, N263Y, D264E, D264G, P265T, D266G, M267K, L268V, V269G, I270F, I270N, G271R, N272H, N272Y, N272T, N272I, F273I, F273V, F273S, F273C, G274R, G274C, G274D, G274A, L275P, L275R, S276C, S276I, S276R, W277R, W277S, N278H, N278D, N278T, N278S, N278K, Q279L, Q279P, Q280E, Q280P, V281I, T282P, Q283K, M284R, M284K, A285S, L286I, L286R, L286P, W287S, A288T, I289N, I289M, M290R, M290K, A291D, A291V, A292D, P293R, F295L, M296R, M296K, S297P, S297Y, S297A, N298Y, D299A, D299V, D299Y, L300R, H302P, H302Q, H302R, I303L, I303M, S304G, S304C, S304R, P305A, P305H, P305L, P305R, P305S, P305T, Q306H, Q306K, Q306R, K308T, A309G, A309S, L310H, L310P, L311H, D313H, D313N, D313A, K314Q, K314R, D315E, A318G, A318S, I319S, I319L, I319V, I319N, N320D, Q321P, D322Y, D322G, P323A, P323H, P323L, P323S, L324M, L324F, L324S, Q327R, Y329S, Q330L, L331I, L331F, R332K, Q333H, Q333K, G334A, D335H, D335N, N336H, N336K, F337I, E338Q, V339L, W340G, W340L, W340S, W340C, E341V, E341G, P343R, P343H, L344I, L344H, S345L, S345T, S345A, G346S, G346R, L347V, L347S, L347F, A348T, A348S, A348G, A348V, W349G, A350D, V351I, V351L, V351G, M353I, M353V, M353R, I354M, I354L, I354V, I354T, N355I, N355T, Q357L, Q357P, Q357H, Q357R, Q357K, E358V, I359M, G360V, G361V, S364T, S364A, S364Y, S364F, Y365C, Y365H, T366A, I367V, I367N, I367T, I367S, A368S, A368E, A368V, V369D, A370S, S371A, S371F, S371P, S371Y, L372M, L372V, G373V, K374N, K374Q, G375V, V376A, A377V, C378F, C378G, C378W, N379H, N379S, N379Y, P380S, A381P, A381S, A381T, A381G, A381V, C382F, C382G, C382S, F383L, F383S, F383V, I384L, I384S, I384V, T385K, T385R, T385S, Q386E, Q386R, L387P, L387V, P389H, P389S, P389T, V390A, V390E, V390G, V390L, R392S, K393M, K393R, L394V, G395V, G395W, F396S, Y397D, E398D, E398V, W399C, W399L, S401P, R402K, L403I, S405C, S405I, S405N, S405T, H406N, H406P, H406Y, N408I, N408K, N408S, P409H, P409R, T410R, G411R, V413A, V413D, V413L, L414M, L414W, L415R, L415V, Q416K, Q416R, L417Q, L417V, E418V, N419H, N419K, T420A, T420I, Q422E, Q422H, Q422K, Q422L, Q422R, M423R, M423V, S424A, S424P, S424T, L425I, L425S, L425V, K426E, K426Q, K426T, K426I, K426N, K426R, D427A, D427H, D427Y, D427E, D427G, D427V, L428F, L428S, L428I, L428V, L429I, L429V, L429F, L429H, and L429P. These mutations are also presented in Table 5 with their corresponding nucleotide changes.

[00105] Exemplary nucleotide changes associated with these novel mutations are shown in Table 5 below:

Table 5

Nucleotide change	Protein change (1 Letter)
c.4C>G	Q2E
c.4C>A	Q2K
c.5A>T	Q2L
c.5A>C	Q2P
c.5A>G	Q2R
c.6G>C	Q2H
c.7C>A	L3M
c.8T>A	L3Q
c.8T>G	L3R
c.10A>G	R4G
c.10A>T	R4W
c.11G>A	R4K
c.11G>C	R4T
c.11G>T	R4M
c.12G>C	R4S
c.14A>T	N5I
c.13A>T	N5Y
c.13A>C	N5H
c.14A>C	N5T
c.14A>G	N5S
c.16C>G	P6A
c.19G>C	E7Q
c.20A>C	E7A
c.20A>G	E7G
c.23T>G	L8R
c.22C>G	L8V
c.25C>G	H9D
c.26A>C	H9P
c.25C>A	H9N
c.32G>C	G11A
c.35G>T	C12F
c.36C>G	C12W
c.37G>T	A13S
c.38C>T	A13V
c.41T>G	L14R
c.40C>A	L14I
c.44C>T	A15V

Table 5

Nucleotide change	Protein change (1 Letter)
c.43G>T	A15S
c.47T>G	L16R
c.46C>A	L16I
c.46C>T	L16F
c.50G>T	R17L
c.52T>G	F18V
c.53T>A	F18Y
c.55C>A	L19M
c.55C>G	L19V
c.56T>G	L19R
c.58G>T	A20S
c.58G>A	A20T
c.61C>A	L21I
c.61C>G	L21V
c.65T>A	V22D
c.67T>G	S23A
c.68C>G	S23C
c.68C>A	S23Y
c.68C>T	S23F
c.71G>T	W24L
c.74A>G	D25G
c.73G>T	D25Y
c.74A>C	D25A
c.75C>G	D25E
c.74A>T	D25V
c.73G>A	D25N
c.76A>T	I26F
c.76A>C	I26L
c.78C>G	I26M
c.77T>G	I26S
c.77T>C	I26T
c.76A>G	I26V
c.80C>A	P27H
c.80C>G	P27R
c.83G>C	G28A
c.83G>T	G28V
c.85G>T	A29S
c.85G>A	A29T
c.89G>T	R30I
c.89G>A	R30K

Table 5

Nucleotide change	Protein change (1 Letter)
c.90A>T	R30S
c.89G>C	R30T
c.91G>A	A31T
c.92C>A	A31E
c.92C>G	A31G
c.91G>C	A31P
c.91G>T	A31S
c.97G>A	D33N
c.101A>T	N34I
c.100A>T	N34Y
c.113G>A	R38K
c.113G>C	R38T
c.115A>C	T39P
c.118C>A	P40T
c.121A>C	T41P
c.127G>T	G43C
c.130T>G	W44G
c.131G>T	W44L
c.130T>A	W44R
c.131G>C	W44S
c.134T>A	L45Q
c.140G>C	W47S
c.143A>G	E48G
c.143A>T	E48V
c.146G>A	R49H
c.148T>A	F50I
c.148T>C or c.150C>G or c.150C>A	F50L
c.149T>C	F50S
c.148T>G	F50V
c.151A>T	M51L
c.155G>T	C52F
c.160C>A	L54I
c.163G>A	D55N
c.166T>C	C56R
c.169C>G	Q57E
c.171G>C	Q57H
c.169C>A	Q57K
c.170A>C	Q57P
c.173A>C	E58A
c.173A>G	E58G

Table 5

Nucleotide change	Protein change (1 Letter)
c.172G>C	E58Q
c.174A>T	E58D
c.173A>T	E58V
c.182A>C	D61A
c.182A>G	D61G
c.181G>C	D61H
c.181G>A	D61N
c.181G>T	D61Y
c.184T>A	S62T
c.188G>T	C63F
c.187T>G	C63G
c.189C>G	C63W
c.190A>T	I64F
c.192C>G	I64M
c.191T>A	I64N
c.191T>G	I64S
c.191T>C	I64T
c.197A>C	E66A
c.200A>G	K67R
c.202C>G	L68V
c.203T>A	L68H
c.203T>C	L68P
c.203T>G	L68R
c.205T>G	F69V
c.206T>G	F69C
c.206T>C	F69S
c.208A>G	M70V
c.209T>C	M70T
c.211G>A	E71K
c.215T>A	M72K
c.217G>C	A73P
c.218C>G	A73G
c.220G>C	E74Q
c.221A>C	E74A
c.223C>G	L75V
c.224T>A	L75H
c.223C>A	L75I
c.224T>G	L75R
c.227T>A	M76K
c.226A>T	M76L

Table 5

Nucleotide change	Protein change (1 Letter)
c.228G>C or c.228G>A or c.228G>T	M76I
c.229G>T	V77F
c.230T>C	V77A
c.230T>G	V77G
c.230T>A	V77D
c.232T>A	S78T
c.232T>G	S78A
c.238G>C	G80R
c.241T>G	W81G
c.244A>C	K82Q
c.247G>T	D83Y
c.247G>C	D83H
c.254G>T	G85V
c.256T>A	Y86N
c.257A>C	Y86S
c.259G>A	E87K
c.260A>C	E87A
c.260A>T	E87V
c.259G>C	E87Q
c.263A>T	Y88F
c.265C>A	L89I
c.269G>T	C90F
c.268T>G	C90G
c.268T>A	C90S
c.271A>G	I91V
c.272T>A	I91N
c.275A>C	D92A
c.276T>A	D92E
c.278A>C	D93A
c.277G>C	D93H
c.280T>C	C94R
c.282T>G	C94W
c.283T>A	W95R
c.287T>A	M96K
c.287T>G	M96R
c.290C>G	A97G
c.292C>G	P98A
c.292C>T	P98S
c.292C>A	P98T
c.297A>T	Q99H

Table 5

Nucleotide change	Protein change (1 Letter)
c.295C>A	Q99K
c.298A>G	R100G
c.299G>T	R100I
c.300A>T	R100S
c.301G>A	D101N
c.301G>T	D101Y
c.308A>C	E103A
c.309A>T	E103D
c.308A>G	E103G
c.307G>A	E103K
c.308A>T	E103V
c.310G>T	G104C
c.310G>C	G104R
c.315A>T	R105S
c.320A>C	Q107P
c.323C>G	A108G
c.322G>C	A108P
c.322G>T	A108S
c.326A>T	D109V
c.329C>A	P110H
c.328C>T	P110S
c.331C>G	Q111E
c.333G>C	Q111H
c.332A>G	Q111R
c.331C>A	Q111K
c.332A>T	Q111L
c.332A>C	Q111P
c.335G>C	R112P
c.338T>G	F113C
c.340C>G	P114A
c.341C>A	P114H
c.340C>T	P114S
c.340C>A	P114T
c.341C>G	P114R
c.344A>T	H115L
c.344A>C	H115P
c.345T>A	H115Q
c.344A>G	H115R
c.343C>T	H115Y
c.346G>T	G116W

Table 5

Nucleotide change	Protein change (1 Letter)
c.347G>C	G116A
c.347G>A	G116E
c.349A>T	I117F
c.349A>C	I117L
c.350T>A	I117N
c.349A>G	I117V
c.352C>G	R118G
c.353G>C	R118P
c.352C>A	R118S
c.353G>T	R118L
c.353G>A	R118H
c.355C>G	Q119E
c.357G>C	Q119H
c.355C>A	Q119K
c.356A>T	Q119L
c.356A>C	Q119P
c.358C>A	L120I
c.359T>A	L120Q
c.359T>G	L120R
c.361G>T	A121S
c.362C>A	A121D
c.362C>G	A121G
c.364A>G	N122D
c.364A>C	N122H
c.365A>T	N122I
c.366T>A	N122K
c.365A>G	N122S
c.365A>C	N122T
c.364A>T	N122Y
c.367T>C	Y123H
c.370G>C	V124L
c.371T>C	V124A
c.370G>T	V124F
c.375C>G	H125Q
c.377G>C	S126T
c.378C>G	S126R
c.377G>A	S126N
c.379A>C	K127Q
c.380A>C	K127T
c.380A>G	K127R

Table 5

Nucleotide change	Protein change (1 Letter)
c.380A>T	K127I
c.381A>T	K127N
c.382G>C	G128R
c.383G>T	G128V
c.385C>A	L129M
c.386T>A	L129Q
c.386T>G	L129R
c.388A>G	K130E
c.389A>C	K130T
c.392T>A	L131Q
c.391C>A	L131I
c.392T>G	L131R
c.394G>T	G132W
c.395G>T	G132V
c.398T>G	I133S
c.400T>A	Y134N
c.401A>G	Y134C
c.401A>T	Y134F
c.403G>C	A135P
c.407A>G	D136G
c.409G>T	V137F
c.413G>T	G138V
c.415A>G	N139D
c.421A>C	T141P
c.421A>G	T141A
c.424T>A	C142S
c.424T>G	C142G
c.425G>T	C142F
c.427G>T	A143S
c.433T>A	F145I
c.439G>T	G147W
c.440G>T	G147V
c.443G>T	S148I
c.445T>A	F149I
c.445T>G	F149V
c.446T>A	F149Y
c.447T>A	F149L
c.446T>C	F149S
c.449G>C	G150A
c.448G>C	G150R

Table 5

Nucleotide change	Protein change (1 Letter)
c.451T>C	Y151H
c.451T>A	Y151N
c.452A>T	Y151F
c.459C>G	D153E
c.458A>G	D153G
c.460A>T	I154F
c.460A>C	I154L
c.462T>G	I154M
c.461T>A	I154N
c.461T>G	I154S
c.461T>C	I154T
c.460A>G	I154V
c.464A>C	D155A
c.464A>G	D155G
c.463G>A	D155N
c.464A>T	D155V
c.463G>T	D155Y
c.466G>C	A156P
c.470A>G	Q157R
c.472A>C	T158P
c.476T>C	F159S
c.478G>C	A160P
c.482A>C	D161A
c.483C>G	D161E
c.482A>G	D161G
c.488G>C	G163A
c.488G>A	G163E
c.487G>C	G163R
c.491T>A	V164E
c.497T>C	L166P
c.497T>G	L166R
c.500T>G	L167R
c.502A>C	K168Q
c.502A>G	K168E
c.503A>T	K168I
c.503A>C	K168T
c.509A>C	D170A
c.510T>A	D170E
c.508G>T	D170Y
c.517T>G	Y173D

Table 5

Nucleotide change	Protein change (1 Letter)
c.517T>A	Y173N
c.521G>T	C174F
c.520T>A	C174S
c.522T>G	C174W
c.521G>A	C174Y
c.524A>C	D175A
c.526A>G	S176G
c.527G>T	S176I
c.527G>A	S176N
c.527G>C	S176T
c.534A>T	E178D
c.533A>T	E178V
c.535A>G	N179D
c.535A>C	N179H
c.536A>T	N179I
c.537T>A	N179K
c.536A>G	N179S
c.536A>C	N179T
c.535A>T	N179Y
c.541G>T	A181S
c.542C>A	A181E
c.542C>G	A181G
c.544G>A	D182N
c.544G>C	D182H
c.550T>G	Y184D
c.554A>G	K185R
c.557A>G	H186R
c.560T>A	M187K
c.565T>A	L189M
c.566T>G	L189W
c.568G>C	A190P
c.572T>G	L191R
c.574A>T	N192Y
c.575A>T	N192I
c.578G>A	R193K
c.579G>C	R193S
c.584G>C	G195A
c.584G>A	G195D
c.589A>G or c.591C>G or c.591C>A	S197R
c.592A>T	I198F

Table 5

Nucleotide change	Protein change (1 Letter)
c.592A>C	I198L
c.593T>A	I198N
c.592A>G	I198V
c.598T>G	Y200D
c.599A>T	Y200F
c.598T>C	Y200H
c.605G>T	C202F
c.604T>G	C202G
c.604T>A	C202S
c.613C>G	P205A
c.614C>A	P205H
c.619T>G	Y207D
c.619T>A	Y207N
c.624G>C	M208I
c.622A>T	M208L
c.623T>C	M208T
c.622A>G	M208V
c.626G>T	W209L
c.626G>C	W209S
c.628C>G	P210A
c.629C>G	P210R
c.631T>A	F211I
c.634C>G	Q212E
c.634C>A	Q212K
c.635A>T	Q212L
c.635A>G	Q212R
c.638A>C	K213T
c.655A>G	I219V
c.658C>G	R220G
c.665A>T	Y222F
c.667T>A or c.668G>C	C223S
c.668G>T	C223F
c.669C>G	C223W
c.672T>A	N224K
c.670A>T	N224Y
c.671A>T	N224I
c.673C>A	H225N
c.673C>T	H225Y
c.674A>C	H225P
c.674A>T	H225L

Table 5

Nucleotide change	Protein change (1 Letter)
c.675C>G	H225Q
c.676T>G	W226G
c.677G>C	W226S
c.677G>T	W226L
c.680G>T	R227L
c.682A>T	N228Y
c.684T>A	N228K
c.685T>G	F229V
c.686T>G	F229C
c.688G>T	A230S
c.691G>C	D231H
c.691G>T	D231Y
c.692A>C	D231A
c.693C>G	D231E
c.695T>A	I232N
c.694A>T	I232F
c.697G>A	D233N
c.697G>C	D233H
c.697G>T	D233Y
c.700G>A	D234N
c.700G>C	D234H
c.701A>C	D234A
c.701A>G	D234G
c.703T>C	S235P
c.706T>G	W236G
c.707G>C	W236S
c.709A>G	K237E
c.711A>T	K237N
c.709A>C	K237Q
c.710A>G	K237R
c.710A>C	K237T
c.716T>A	I239K
c.716T>G	I239R
c.715A>G	I239V
c.718A>C	K240Q
c.719A>C	K240T
c.721A>G	S241G
c.722G>A	S241N
c.723T>A	S241R
c.733T>A	W245R

Table 5

Nucleotide change	Protein change (1 Letter)
c.734G>C	W245S
c.736A>C	T246P
c.736A>T	T246S
c.742T>A	F248I
c.743T>C	F248S
c.752A>C	E251A
c.753G>C	E251D
c.755G>T	R252I
c.755G>A	R252K
c.756A>T	R252S
c.759T>G	I253M
c.757A>C	I253L
c.760G>A	V254I
c.760G>C	V254L
c.764A>G	D255G
c.766G>T	V256F
c.766G>A	V256I
c.767T>C	V256A
c.773G>C	G258A
c.778G>C or c.778G>A	G260R
c.779G>T	G260V
c.784T>A or c.784T>C	W262R
c.784T>G	W262G
c.785G>C	W262S
c.787A>G	N263D
c.788A>T	N263I
c.789T>A or c.789T>G	N263K
c.787A>T	N263Y
c.792C>G	D264E
c.791A>G	D264G
c.793C>A	P265T
c.797A>G	D266G
c.800T>A	M267K
c.802T>G	L268V
c.806T>G	V269G
c.808A>T	I270F
c.809T>A	I270N
c.811G>C	G271R
c.814A>C	N272H
c.814A>T	N272Y

Table 5

Nucleotide change	Protein change (1 Letter)
c.815A>C	N272T
c.815A>T	N272I
c.817T>A	F273I
c.817T>G	F273V
c.818T>C	F273S
c.818T>G	F273C
c.820G>C	G274R
c.820G>T	G274C
c.821G>A	G274D
c.821G>C	G274A
c.824T>C	L275P
c.824T>G	L275R
c.826A>T	S276C
c.827G>T	S276I
c.828C>A or c.828C>G	S276R
c.829T>A	W277R
c.830G>C	W277S
c.832A>C	N278H
c.832A>G	N278D
c.833A>C	N278T
c.833A>G	N278S
c.834T>G or c.834T>A	N278K
c.836A>T	Q279L
c.836A>C	Q279P
c.838C>G	Q280E
c.839A>C	Q280P
c.841G>A	V281I
c.844A>C	T282P
c.847C>A	Q283K
c.851T>G	M284R
c.851T>A	M284K
c.853G>T	A285S
c.856C>A	L286I
c.857T>G	L286R
c.857T>C	L286P
c.860G>C	W287S
c.862G>A	A288T
c.866T>A	I289N
c.867C>G	I289M
c.869T>G	M290R

Table 5

Nucleotide change	Protein change (1 Letter)
c.869T>A	M290K
c.872C>A	A291D
c.872C>T	A291V
c.875C>A	A292D
c.878C>G	P293R
c.885C>G	F295L
c.887T>G	M296R
c.887T>A	M296K
c.889T>C	S297P
c.890C>A	S297Y
c.889T>G	S297A
c.892A>T	N298Y
c.896A>C	D299A
c.896A>T	D299V
c.895G>T	D299Y
c.899T>G	L300R
c.905A>C	H302P
c.906C>G	H302Q
c.905A>G	H302R
c.907A>C	I303L
c.909C>G	I303M
c.910A>G	S304G
c.910A>T	S304C
c.912C>G	S304R
c.913C>G	P305A
c.914C>A	P305H
c.914C>T	P305L
c.914C>G	P305R
c.913C>T	P305S
c.913C>A	P305T
c.918A>T	Q306H
c.916C>A	Q306K
c.917A>G	Q306R
c.923A>C	K308T
c.926C>G	A309G
c.925G>T	A309S
c.929T>A	L310H
c.929T>C	L310P
c.932T>A	L311H
c.937G>C	D313H

Table 5

Nucleotide change	Protein change (1 Letter)
c.937G>A	D313N
c.938A>C	D313A
c.940A>C	K314Q
c.941A>G	K314R
c.945C>G	D315E
c.953C>G	A318G
c.952G>T	A318S
c.956T>G	I319S
c.955A>C	I319L
c.955A>G	I319V
c.956T>A	I319N
c.958A>G	N320D
c.962A>C	Q321P
c.964G>T	D322Y
c.965A>G	D322G
c.967C>G	P323A
c.968C>A	P323H
c.968C>T	P323L
c.967C>T	P323S
c.970T>A	L324M
c.972G>C	L324F
c.971T>C	L324S
c.980A>G	Q327R
c.986A>C	Y329S
c.989A>T	Q330L
c.991C>A	L331I
c.991C>T	L331F
c.995G>A	R332K
c.999G>C	Q333H
c.997C>A	Q333K
c.1001G>C	G334A
c.1003G>C	D335H
c.1003G>A	D335N
c.1006A>C	N336H
c.1008C>G	N336K
c.1009T>A	F337I
c.1012G>C	E338Q
c.1015G>C	V339L
c.1018T>G	W340G
c.1019G>T	W340L

Table 5

Nucleotide change	Protein change (1 Letter)
c.1019G>C	W340S
c.1020G>C	W340C
c.1022A>T	E341V
c.1022A>G	E341G
c.1028C>G	P343R
c.1028C>A	P343H
c.1030C>A	L344I
c.1031T>A	L344H
c.1034C>T	S345L
c.1033T>A	S345T
c.1033T>G	S345A
c.1036G>A	G346S
c.1036G>C	G346R
c.1039T>G	L347V
c.1040T>C	L347S
c.1041A>T	L347F
c.1042G>A	A348T
c.1042G>T	A348S
c.1043C>G	A348G
c.1043C>T	A348V
c.1045T>G	W349G
c.1049C>A	A350D
c.1051G>A	V351I
c.1051G>C	V351L
c.1052T>G	V351G
c.1059G>C	M353I
c.1057A>G	M353V
c.1058T>G	M353R
c.1062A>G	I354M
c.1060A>T	I354L
c.1060A>G	I354V
c.1061T>C	I354T
c.1064A>T	N355I
c.1064A>C	N355T
c.1070A>T	Q357L
c.1070A>C	Q357P
c.1071G>C	Q357H
c.1070A>G	Q357R
c.1069C>A	Q357K
c.1073A>T	E358V

Table 5

Nucleotide change	Protein change (1 Letter)
c.1077T>G	I359M
c.1079G>T	G360V
c.1082G>T	G361V
c.1090T>A	S364T
c.1090T>G	S364A
c.1091C>A	S364Y
c.1091C>T	S364F
c.1094A>G	Y365C
c.1093T>C	Y365H
c.1096A>G	T366A
c.1099A>G	I367V
c.1100T>A	I367N
c.1100T>C	I367T
c.1100T>G	I367S
c.1102G>T	A368S
c.1103C>A	A368E
c.1103C>T	A368V
c.1106T>A	V369D
c.1108G>T	A370S
c.1111T>G	S371A
c.1112C>T	S371F
c.1111T>C	S371P
c.1112C>A	S371Y
c.1114C>A	L372M
c.1114C>G	L372V
c.1118G>T	G373V
c.1122A>T	K374N
c.1120A>C	K374Q
c.1124G>T	G375V
c.1127T>C	V376A
c.1130C>T	A377V
c.1133G>T	C378F
c.1132T>G	C378G
c.1134T>G	C378W
c.1135A>C	N379H
c.1136A>G	N379S
c.1135A>T	N379Y
c.1138C>T	P380S
c.1141G>C	A381P
c.1141G>T	A381S

Table 5

Nucleotide change	Protein change (1 Letter)
c.1141G>A	A381T
c.1142C>G	A381G
c.1142C>T	A381V
c.1145G>T	C382F
c.1144T>G	C382G
c.1144T>A	C382S
c.1147T>C or c.1149C>G or c.1149C>A	F383L
c.1148T>C	F383S
c.1147T>G	F383V
c.1150A>C	I384L
c.1151T>G	I384S
c.1150A>G	I384V
c.1154C>A	T385K
c.1154C>G	T385R
c.1153A>T	T385S
c.1156C>G	Q386E
c.1157A>G	Q386R
c.1160T>C	L387P
c.1159C>G	L387V
c.1166C>A	P389H
c.1165C>T	P389S
c.1165C>A	P389T
c.1169T>C	V390A
c.1169T>A	V390E
c.1169T>G	V390G
c.1168G>C	V390L
c.1176G>C	R392S
c.1178A>T	K393M
c.1178A>G	K393R
c.1180C>G	L394V
c.1184G>T	G395V
c.1183G>T	G395W
c.1187T>C	F396S
c.1189T>G	Y397D
c.1194A>T	E398D
c.1193A>T	E398V
c.1197G>C	W399C
c.1196G>T	W399L
c.1201T>C	S401P
c.1205G>A	R402K

Table 5

Nucleotide change	Protein change (1 Letter)
c.1207T>A	L403I
c.1213A>T	S405C
c.1214G>T	S405I
c.1214G>A	S405N
c.1214G>C	S405T
c.1216C>A	H406N
c.1217A>C	H406P
c.1216C>T	H406Y
c.1223A>T	N408I
c.1224T>A	N408K
c.1223A>G	N408S
c.1226C>A	P409H
c.1226C>G	P409R
c.1229C>G	T410R
c.1231G>C	G411R
c.1238T>C	V413A
c.1238T>A	V413D
c.1237G>C	V413L
c.1240T>A	L414M
c.1241T>G	L414W
c.1244T>G	L415R
c.1243C>G	L415V
c.1246C>A	Q416K
c.1247A>G	Q416R
c.1250T>A	L417Q
c.1249C>G	L417V
c.1253A>T	E418V
c.1255A>C	N419H
c.1257T>A	N419K
c.1258A>G	T420A
c.1259C>T	T420I
c.1264C>G	Q422E
c.1266G>C	Q422H
c.1264C>A	Q422K
c.1265A>T	Q422L
c.1265A>G	Q422R
c.1268T>G	M423R
c.1267A>G	M423V
c.1270T>G	S424A
c.1270T>C	S424P

Table 5

Nucleotide change	Protein change (1 Letter)
c.1270T>A	S424T
c.1273T>A	L425I
c.1274T>C	L425S
c.1273T>G	L425V
c.1276A>G	K426E
c.1276A>C	K426Q
c.1277A>C	K426T
c.1277A>T	K426I
c.1278A>T	K426N
c.1277A>G	K426R
c.1280A>C	D427A
c.1279G>C	D427H
c.1279G>T	D427Y
c.1281C>G	D427E
c.1280A>G	D427G
c.1280A>T	D427V
c.1284A>T	L428F
c.1283T>C	L428S
c.1282T>A	L428I
c.1282T>G	L428V
c.1285C>A	L429I
c.1285C>G	L429V
c.1285C>T	L429F
c.1286T>A	L429H
c.1286T>C	L429P

[00106] While the non-amenable mutations presented in Table 5 were initially prophetic non-amenable mutations evaluated by HEK assay, later-identified patients have since presented with several of these mutations. Accordingly, the mutations listed in Table 6 are now patient-associated amenable mutations, thus confirming that the prophetic mutations described herein may later present in patients.

Table 6

Nucleotide change	Protein change (1 Letter)
c.47T>G	L16R
c.146G>A	R49H
c.148T>C or c.150C>G or c.150C>A	F50L

Table 6

Nucleotide change	Protein change (1 Letter)
c.155G>T	C52F
c.188G>T	C63F
c.206T>C	F69S
c.208A>G	M70V
c.228G>C or c.228G>A or c.228G>T	M76I
c.241T>G	W81G
c.254G>T	G85V
c.338T>G	F113C
c.346G>T	G116W
c.359T>G	L120R
c.383G>T	G128V
c.386T>G	L129R
c.388A>G	K130E
c.389A>C	K130T
c.392T>A	L131Q
c.409G>T	V137F
c.421A>G	T141A
c.424T>A	C142S
c.440G>T	G147V
c.443G>T	S148I
c.476T>C	F159S
c.478G>C	A160P
c.487G>C	G163R
c.497T>C	L166P
c.502A>C	K168Q
c.550T>G	Y184D
c.574A>T	N192Y
c.605G>T	C202F
c.613C>G	P205A
c.667T>A or c.668G>C	C223S
c.668G>T	C223F
c.674A>C	H225P
c.676T>G	W226G
c.680G>T	R227L
c.685T>G	F229V
c.691G>T	D231Y
c.692A>C	D231A
c.700G>A	D234N
c.701A>G	D234G
c.706T>G	W236G

Table 6

Nucleotide change	Protein change (1 Letter)
c.743T>C	F248S
c.778G>C or c.778G>A	G260R
c.784T>A or c.784T>C	W262R
c.785G>C	W262S
c.787A>G	N263D
c.789T>A or c.789T>G	N263K
c.793C>A	P265T
c.797A>G	D266G
c.808A>T	I270F
c.815A>C	N272T
c.815A>T	N272I
c.818T>C	F273S
c.820G>C	G274R
c.820G>T	G274C
c.821G>A	G274D
c.826A>T	S276C
c.827G>T	S276I
c.828C>A or c.828C>G	S276R
c.834T>G or c.834T>A	N278K
c.857T>C	L286P
c.887T>A	M296K
c.889T>C	S297P
c.890C>A	S297Y
c.896A>T	D299V
c.929T>C	L310P
c.980A>G	Q327R
c.1019G>C	W340S
c.1022A>G	E341G
c.1058T>G	M353R
c.1124G>T	G375V
c.1133G>T	C378F
c.1147T>C or c.1149C>G or c.1149C>A	F383L
c.1160T>C	L387P
c.1165C>T	P389S

[00107] Furthermore, various embodiments of the present invention provide PCs for the treatment of Fabry disease in a patient having a mutation in the gene encoding α-Gal A, wherein the patient is identified as having a missense mutation in a human α-Gal A encoded by a nucleic acid sequence set forth in SEQ ID NO: 1 and/or SEQ ID NO: 3. Another aspect of the

invention pertains a method of treating a patient diagnosed with Fabry disease. In one or more embodiments, the method comprises administering to a patient a therapeutically effective dose of a PC of α-Gal A. In further embodiments, the patient has a missense mutation in the nucleic acid sequence encoding α-Gal A. Another aspect of the invention pertains to a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease. In one or more embodiments, the method comprises administering to a patient a therapeutically effective dose of a PC of α-Gal A, wherein the patient has a mutant α-Gal A encoded by a nucleic acid sequence having a missense mutation relative to SEQ ID NO: 1 and/or SEQ ID NO: 3. Details and further embodiments of these uses and methods follows below. Any of the embodiments relating a method of treating a patient with Fabry disease, a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease, use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease wherein the patient is identified as having a missense mutation in a human α-Gal A encoded by a nucleic acid sequence set forth in SEQ ID NO: 1 and/or SEQ ID NO: 3 can be combined with any of the other embodiments of the invention, for example embodiments relating to the PCs and suitable dosages thereof.

[00108] In one or more embodiments, the patient may have other mutations in their GLA gene. For example, there may be mutations in the intron region which may or may not affect the resulting α-Gal A enzyme. Thus, in one or more embodiments, the patient has mutant α-Gal A encoded by a nucleic acid sequence having at least 95, 96, 97, 98, 99, 99.1, 99.2, 99.3, 99.4, 99.5, 99.6, 99.7, 99.8 or 99.9% identity to SEQ ID NO: 1. Furthermore, the patient may have one or more additional mutations in the coding region of the GLA gene. Thus, in one or more embodiments, the patient has mutant α-Gal A encoded by a nucleic acid sequence having at least 95, 96, 97, 98, 99, 99.1, 99.2, 99.3, 99.4, 99.5, 99.6, 99.7, 99.8 or 99.9% identity to SEQ ID NO: 3. Moreover, in one or more embodiments, the patient has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20 or 30 mutations relative to SEQ ID NO: 1 or SEQ ID NO: 3. It is also noted that some nucleic acid mutations in SEQ ID NO: 1 or SEQ ID NO: 3 can result in no change in amino acid for the resulting protein, as various amino acids are encoded by multiple nucleic acid sequences. Again, any of these embodiments can be combined with any of the other embodiments of the invention, for example embodiments relating to amenable mutations, the PCs and suitable dosages thereof.

[00109] In various embodiments, a pharmacological reference table is provided that includes one or more of the mutations discloses herein. In one or more embodiments, the pharmacological reference table includes one or more of the mutations from Table 2. In one or more embodiments, the pharmacological reference table includes all of the mutations from Table 2. In one or more embodiments, pharmacological reference table includes one or more of the mutations from Table 1. In one or more embodiments, the pharmacological reference table includes all of the mutations from Table 1. In one or more embodiments, the pharmacological reference table includes one or more of the mutations from Table 1 and one or more of the mutations from Table 2. In one or more embodiments, the pharmacological reference table includes all of the mutations from Table 1 and one or more of the mutations from Table 2. In one or more embodiments, the pharmacological reference table includes one or more of the mutations from Table 1 and all of the mutations from Table 2. In one or more embodiments, the pharmacological reference table includes all of the mutations from Table 1 and all of the mutations from Table 2.

[00110] As described above, the pharmacological reference table can be any publicly accessible written or electronic record. In one or more embodiments, the pharmacological reference table is a written record. In one or more embodiments, the pharmacological reference table is provided in a product label for a migalastat product, such as a migalastat product approved by a US or other regulatory agency for the treatment of Fabry disease. In one or more embodiments, the pharmacological reference table is provided in a product label for GALAFOLD®. In one or more embodiments, the pharmacological reference table is an electronic record. In one or more embodiments, the pharmacological reference table is provided at a website. In one or more embodiments, the website is associated with a migalastat product, such as a migalastat product approved by a US or other regulatory agency for the treatment of Fabry disease. In one or more embodiments, the pharmacological reference table is provided at www.galafoldamenabilitytable.com. In one or more embodiments, the pharmacological reference table is provided at www.fabrygenevariantsearch.com.

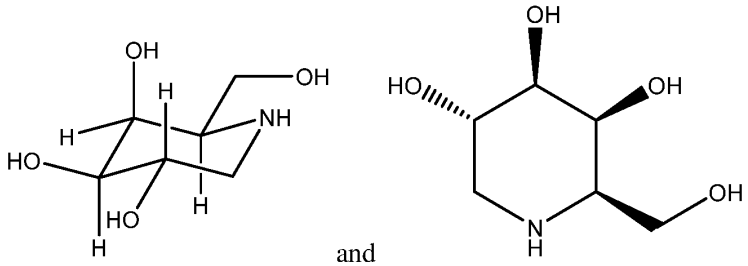
[00111] Various embodiments also relate to a data store including a pharmacological reference table as described herein. Such a data store can include an electronic searching function for determining whether a particular mutation is included in the pharmacological reference table. In one or more embodiments, the data store and optional search function is provided at a website. In one or more embodiments, the data store and optional search function

is provided in an electronic storage medium. Examples of such electronic storage media include, but are not limited to, compact discs (CDs), digital versatile discs (DVDs) hard drives and flash drives.

[00112] Pharmacological Chaperones

[00113] The binding of small molecule inhibitors of enzymes associated with LSDs can increase the stability of both mutant enzyme and the corresponding wild-type enzyme (see U.S. Pat. Nos. 6,274,597; 6,583,158; 6,589,964; 6,599,919; 6,916,829, and 7,141,582 all incorporated herein by reference). In particular, administration of small molecule derivatives of glucose and galactose, which are specific, selective competitive inhibitors for several target lysosomal enzymes, effectively increased the stability of the enzymes in cells *in vitro* and, thus, increased trafficking of the enzymes to the lysosome. Thus, by increasing the amount of enzyme in the lysosome, hydrolysis of the enzyme substrates is expected to increase. The original theory behind this strategy was as follows: since the mutant enzyme protein is unstable in the ER (Ishii et al., *Biochem. Biophys. Res. Comm.* 1996; 220: 812-815), the enzyme protein is retarded in the normal transport pathway (ER→Golgi apparatus→endosomes→lysosome) and prematurely degraded. Therefore, a compound which binds to and increases the stability of a mutant enzyme, may serve as a "chaperone" for the enzyme and increase the amount that can exit the ER and move to the lysosomes. In addition, because the folding and trafficking of some wild-type proteins is incomplete, with up to 70% of some wild-type proteins being degraded in some instances prior to reaching their final cellular location, the chaperones can be used to stabilize wild-type enzymes and increase the amount of enzyme which can exit the ER and be trafficked to lysosomes.

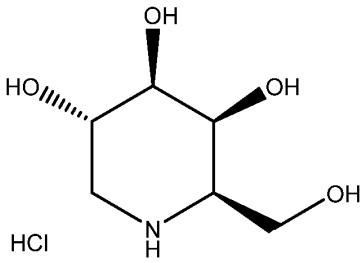
[00114] In one or more embodiments, the pharmacological chaperone comprises migalastat or a salt thereof. The compound migalastat, also known as 1-deoxygalactonojirimycin (1-DGJ) or (2R,3S,4R,5S)-2-(hydroxymethyl) piperdine-3,4,5-triol is a compound having the following chemical formula:



and

Migalastat free base

[00115] As discussed herein, pharmaceutically acceptable salts of migalastat may also be used in the present invention. When a salt of migalastat is used, the dosage of the salt will be adjusted so that the dose of migalastat received by the patient is equivalent to the amount which would have been received had the migalastat free base been used. One example of a pharmaceutically acceptable salt of migalastat is migalastat HCl:



Migalastat HCl

[00116] Migalastat is a low molecular weight iminosugar and is an analogue of the terminal galactose of GL-3. *In vitro* and *in vivo* pharmacologic studies have demonstrated that migalastat acts as a pharmacological chaperone, selectively and reversibly binding, with high affinity, to the active site of wild-type α-Gal A and specific mutant forms of α-Gal A. Migalastat binding stabilizes these mutant forms of α-Gal A in the endoplasmic reticulum facilitating their proper trafficking to lysosomes where dissociation of migalastat allows α-Gal A to reduce the level of GL-3 and other substrates.

[00117] In a specific embodiment, the PC comprises migalastat or salt thereof. In further embodiments, the PC comprises migalastat hydrochloride.

[00118] Any of these PCs for α-Gal A may be used in combination with any of the other embodiments of the invention, for example embodiments relating to a method of treating a patient with Fabry disease, a method of enhancing α-Gal A in a patient diagnosed with or suspected of having Fabry disease, use of a pharmacological chaperone for α-Gal A for the

manufacture of a medicament for treating a patient diagnosed with Fabry disease or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease as well as embodiments relating to suitable doses of PCs, amenable mutations and to the treatment of a Fabry patient having certain mutations in the nucleic acid sequence encoding α-Gal A.

[00119] Dosing, Formulation and Administration

[00120] In one or more embodiments, the Fabry patient is administered migalastat or salt thereof at a frequency of once every other day (also referred to as "QOD"). In various embodiments, the doses described herein pertain to migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt. In some embodiments, these doses pertain to the free base of migalastat. In alternate embodiments, these doses pertain to a salt of migalastat. In further embodiments, the salt of migalastat is migalastat hydrochloride. The administration of migalastat or a salt of migalastat is referred to herein as "migalastat therapy".

[00121] The effective amount of migalastat or salt thereof can be in the range from about 100 mg FBE to about 150 mg FBE. Exemplary doses include about 100 mg FBE, about 105 mg FBE, about 110 mg FBE, about 115 mg FBE, about 120 mg FBE, about 123 mg FBE, about 125 mg FBE, about 130 mg FBE, about 135 mg FBE, about 140 mg FBE, about 145 mg FBE or about 150 mg FBE.

[00122] Again, it is noted that 150 mg of migalastat hydrochloride is equivalent to 123 mg of the free base form of migalastat. Thus, in one or more embodiments, the dose is 150 mg of migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt, administered at a frequency of once every other day. As set forth above, this dose is referred to as 123 mg FBE of migalastat. In further embodiments, the dose is 150 mg of migalastat hydrochloride administered at a frequency of once every other day. In other embodiments, the dose is 123 mg of the migalastat free base administered at a frequency of once every other day.

[00123] In various embodiments, the effective amount is about 122 mg, about 128 mg, about 134 mg, about 140 mg, about 146 mg, about 150 mg, about 152 mg, about 159 mg, about 165 mg, about 171 mg, about 177 mg or about 183 mg of migalastat hydrochloride.

[00124] Accordingly, in various embodiments, migalastat therapy includes administering 123 mg FBE at a frequency of once every other day, such as 150 mg of migalastat hydrochloride every other day.

[00125] The administration of migalastat or salt thereof may be for a certain period of time. In one or more embodiments, the migalastat or salt thereof is administered for a duration of at least 28 days, such as at least 30, 60 or 90 days or at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 16, 20, 24, 30 or 36 months or at least 1, 2, 3, 4 or 5 years. In various embodiments, the migalastat therapy is long-term migalastat therapy of at least 6 months, such as at least 6, 7, 8, 9, 10, 11, 12, 16, 20, 24, 30 or 36 months or at least 1, 2, 3, 4 or 5 years.

[00126] Administration of migalastat or salt thereof according to the present invention may be in a formulation suitable for any route of administration, but is preferably administered in an oral dosage form such as a tablet, capsule or solution. As one example, the patient is orally administered capsules each containing 150 mg migalastat hydrochloride or an equivalent dose of migalastat or a salt thereof other than the hydrochloride salt.

[00127] In some embodiments, the PC (*e.g.*, migalastat or salt thereof) is administered orally. In one or more embodiments, the PC (*e.g.*, migalastat or salt thereof) is administered by injection. The PC may be accompanied by a pharmaceutically acceptable carrier, which may depend on the method of administration.

[00128] In one or more embodiments, the PC (*e.g.*, migalastat or salt thereof) is administered as monotherapy, and can be in a form suitable for any route of administration, including *e.g.*, orally in the form tablets or capsules or liquid, or in sterile aqueous solution for injection. In other embodiments, the PC is provided in a dry lyophilized powder to be added to the formulation of the replacement enzyme during or immediately after reconstitution to prevent enzyme aggregation *in vitro* prior to administration.

[00129] When the PC (*e.g.*, migalastat or salt thereof) is formulated for oral administration, the tablets or capsules can be prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (*e.g.*, pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (*e.g.*, lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (*e.g.*, magnesium stearate, talc or silica); disintegrants (*e.g.*, potato starch or sodium starch glycolate); or wetting agents (*e.g.*, sodium lauryl sulfate). The tablets may be coated by methods well known in the art. Liquid preparations for oral administration may take the form of, for example, solutions,

syrups or suspensions, or they may be presented as a dry product for constitution with water or another suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (*e.g.*, sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (*e.g.*, lecithin or acacia); non-aqueous vehicles (*e.g.*, almond oil, oily esters, ethyl alcohol or fractionated vegetable oils); and preservatives (*e.g.*, methyl or propyl-p- hydroxybenzoates or sorbic acid). The preparations may also contain buffer salts, flavoring, coloring and sweetening agents as appropriate. Preparations for oral administration may be suitably formulated to give controlled release of the active chaperone compound.

[00130] The pharmaceutical formulations of the PC (*e.g.*, migalastat or salt thereof) suitable for parenteral/injectable use generally include sterile aqueous solutions (where water soluble), or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. In all cases, the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, benzyl alcohol, sorbic acid, and the like. In many cases, it will be reasonable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monosterate and gelatin.

[00131] Sterile injectable solutions are prepared by incorporating the purified enzyme (if any) and the PC (*e.g.*, migalastat or salt thereof) in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filter or terminal sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are

vacuum drying and the freeze-drying technique which yield a powder of the active ingredient plus any additional desired ingredient from previously sterile-filtered solution thereof.

[00132] The formulation can contain an excipient. Pharmaceutically acceptable excipients which may be included in the formulation are buffers such as citrate buffer, phosphate buffer, acetate buffer, bicarbonate buffer, amino acids, urea, alcohols, ascorbic acid, and phospholipids; proteins, such as serum albumin, collagen, and gelatin; salts such as EDTA or EGTA, and sodium chloride; liposomes; polyvinylpyrollidone; sugars, such as dextran, mannitol, sorbitol, and glycerol; propylene glycol and polyethylene glycol (*e.g.*, PEG-4000, PEG-6000); glycerol; glycine or other amino acids; and lipids. Buffer systems for use with the formulations include citrate; acetate; bicarbonate; and phosphate buffers. Phosphate buffer is a preferred embodiment.

[00133] The route of administration of the chaperone compound may be oral or parenteral, including intravenous, subcutaneous, intra-arterial, intraperitoneal, ophthalmic, intramuscular, buccal, rectal, vaginal, intraorbital, intracerebral, intradermal, intracranial, intraspinal, intraventricular, intrathecal, intracisternal, intracapsular, intrapulmonary, intranasal, transmucosal, transdermal, or via inhalation.

[00134] Administration of the above-described parenteral formulations of the chaperone compound may be by periodic injections of a bolus of the preparation, or may be administered by intravenous or intraperitoneal administration from a reservoir which is external (*e.g.*, an i.v. bag) or internal (*e.g.*, a bioerodable implant).

[00135] Embodiments relating to pharmaceutical formulations and administration may be combined with any of the other embodiments of the invention, for example embodiments relating to methods of treating patients with Fabry disease, use of a pharmacological chaperone for α-Gal A for the manufacture of a medicament for treating a patient diagnosed with Fabry disease or to a pharmacological chaperone for α-Gal A for use in treating a patient diagnosed with Fabry disease as well as embodiments relating to amenable mutations, the PCs and suitable dosages thereof.

[00136] In one or more embodiments, the PC (*e.g.*, migalastat or salt thereof) is administered in combination with ERT. ERT increases the amount of protein by exogenously introducing wild-type or biologically functional enzyme by way of infusion. This therapy has been developed for many genetic disorders, including LSDs such as Fabry disease, as referenced above. After the infusion, the exogenous enzyme is expected to be taken up by

tissues through non-specific or receptor-specific mechanism. In general, the uptake efficiency is not high, and the circulation time of the exogenous protein is short. In addition, the exogenous protein is unstable and subject to rapid intracellular degradation as well as having the potential for adverse immunological reactions with subsequent treatments. In one or more embodiments, the chaperone is administered at the same time as replacement enzyme (*e.g.*, replacement α-Gal A). In some embodiments, the chaperone is co-formulated with the replacement enzyme (*e.g.*, replacement α-Gal A).

[00137] Reference throughout this specification to "one embodiment," "certain embodiments," "various embodiments," "one or more embodiments" or "an embodiment" means that a particular feature, structure, material, or characteristic described in connection with the embodiment is included in at least one embodiment of the invention. Thus, the appearances of the phrases such as "in one or more embodiments," "in certain embodiments," "in various embodiments," "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily referring to the same embodiment of the invention. Furthermore, the particular features, structures, materials, or characteristics may be combined in any suitable manner in one or more embodiments.

[00138] Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It will be apparent to those skilled in the art that various modifications and variations can be made to the method and apparatus of the present invention without departing from the spirit and scope of the invention. Thus, it is intended that the present invention include modifications and variations that are within the scope of the appended claims and their equivalents.

EXAMPLE: Effect of Migalastat on Mutations of α-Gal A

[00139] The α-Gal A activity was measured in lysates prepared from HEK-293 cells transiently transfected with the indicated mutant form of α-Gal A and incubated in the absence or presence of 10 μM migalastat for 5 days. The α-Gal A activity is expressed as the nmoles of free 4-MU released per milligram of protein per hour (nmol/mg/hr). Baseline α-Gal A activity and α-Gal A activity after incubation with l0 μM migalastat, were additionally expressed as a percentage of baseline wild-type α-Gal A activity (% WT). The wild-type α-Gal A activity that

was used to calculate these percentages was the average activity measured in lysates from wild-type transfected cells, incubated in the absence of migalastat, measured in parallel.

[00140] The results of the α-Gal A activity testing for the novel mutations presented in Table 2 is shown in Table 7 below:

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
N5D	26578 ± 1944	34661 ± 1816	0.0017	74.9 ± 5.1	98.9 ± 5.5	24.1	1.3
N5K	22221 ± 753	27689 ± 955	0.0002	58.6 ± 2.6	73 ± 3.3	14.4	1.3
P6L	18599 ± 1034	24229 ± 1870	0.0158	49.2 ± 3.1	63.4 ± 5	14.2	1.3
P6Q	17261 ± 825	22316 ± 1261	0.0013	49.4 ± 2.2	64.8 ± 4.3	15.4	1.3
P6R	24240 ± 1350	32919 ± 1593	0.0003	70.1 ± 4.2	94.1 ± 3.6	24.0	1.4
P6S	34848 ± 1440	43046 ± 1713	0.0009	82 ± 2.9	101.5 ± 3.7	19.5	1.2
P6T	30926 ± 1479	37354 ± 1577	0.0077	88.3 ± 3.3	108 ± 5.1	19.7	1.2
E7D	31325 ± 1280	39271 ± 1669	0.0005	77.6 ± 2.3	97.2 ± 3	19.6	1.3
E7K	18705 ± 801	25316 ± 1403	0.0001	55.2 ± 3.1	75.4 ± 5.7	20.2	1.4
E7V	25273 ± 1376	30825 ± 1805	0.0193	74.7 ± 2.8	91.6 ± 4.3	16.9	1.2
L8I	21345 ± 1469	26036 ± 1514	0.0090	67.5 ± 4.2	82.4 ± 4.3	14.9	1.2
L8P	19934 ± 3444	25868 ± 4321	0.0028	55.1 ± 6.9	72.3 ± 8.5	17.2	1.3
L8Q	18234 ± 1818	22878 ± 1755	0.0053	57.5 ± 5.4	72.3 ± 5.1	14.7	1.3
H9L	26490 ± 1295	36318 ± 2304	0.0003	75.9 ± 5.5	107.8 ± 11.2	31.9	1.4
H9Q	20382 ± 918	27072 ± 1062	0.0001	57.3 ± 2.9	78.2 ± 5.6	20.9	1.3
H9R	21497 ± 2019	27866 ± 1854	0.0042	56.2 ± 4.2	75.2 ± 5.4	19.0	1.3
H9Y	27713 ± 2168	33834 ± 2369	0.0090	81.9 ± 8.5	101 ± 10	19.1	1.2
L10M	19028 ± 958	26110 ± 1344	0.0001	55.1 ± 4.1	78.3 ± 6.8	23.2	1.4
L10P	21054 ± 1238	26571 ± 1812	0.0042	68.3 ± 3.9	85.9 ± 5.5	17.5	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
L10Q	14594 ± 970	20723 ± 1583	0.0013	47.8 ± 3.3	67.3 ± 5.4	19.5	1.4
L10R	15760 ± 920	24293 ± 2170	0.0017	51.9 ± 3.3	78.9 ± 7.7	27.0	1.5
L10V	17475 ± 683	23595 ± 1256	0.0001	49.5 ± 2.6	68.8 ± 6.1	19.3	1.4
G11C	34393 ± 2207	43933 ± 3128	0.0049	111.9 ± 7.3	142.3 ± 10.3	30.4	1.3
G11D	13315 ± 1237	18851 ± 1704	0.0142	43.9 ± 4.3	61.3 ± 5.8	17.3	1.4
G11R	32525 ± 2047	41260 ± 3644	0.0339	105.2 ± 6.1	134.3 ± 12.7	29.1	1.3
G11S	28169 ± 1641	38524 ± 3460	0.0072	91 ± 4.9	122.9 ± 10.8	31.9	1.4
G11V	39507 ± 1757	49059 ± 1869	0.0010	121.8 ± 7	153 ± 9.2	31.3	1.2
C12G	14560 ± 1307	21780 ± 2916	0.0234	44.4 ± 3.1	64.7 ± 6.9	20.3	1.5
C12R	10869 ± 1110	16596 ± 2243	0.0128	32.9 ± 2.6	49.1 ± 5.3	16.2	1.5
C12S	15741 ± 1462	23071 ± 2829	0.0219	47.6 ± 3.2	68.6 ± 6.4	21.0	1.5
C12Y	32218 ± 2218	38717 ± 2744	0.0339	99.8 ± 5.9	118.6 ± 7.4	18.9	1.2
A13E	16631 ± 1310	23633 ± 2424	0.0083	51.2 ± 3.5	71.5 ± 6	20.2	1.4
A13G	21739 ± 1693	27200 ± 2187	0.0360	67 ± 4.3	83.6 ± 5.5	16.6	1.3
L14F	30970 ± 2383	38206 ± 2599	0.0283	97.4 ± 5.3	122.1 ± 7.4	24.7	1.2
L14H	1316 ± 125	3166 ± 428	0.0022	3.8 ± 0.2	8.8 ± 1	5.0	2.4
L14V	25550 ± 1778	31818 ± 1959	0.0249	82.5 ± 5.2	101.6 ± 5.1	19.1	1.3
R17C	33909 ± 1965	48618 ± 2267	0.0001	97.2 ± 5.8	140.5 ± 8.4	43.3	1.4
R17G	40647 ± 2328	50772 ± 2273	0.0028	117 ± 7.1	145.2 ± 6.2	28.2	1.3
R17H	32181 ± 2325	47769 ± 2358	0.0001	91.7 ± 6	138.1 ± 8.8	46.4	1.5
R17P	28074 ± 1526	45995 ± 2671	0.0001	80.6 ± 4.7	133.4 ± 9.9	52.8	1.6
R17S	28809 ± 1251	42089 ± 1807	0.0001	82.1 ± 3.1	121.4 ± 6.6	39.4	1.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
F18I	38335 ± 2361	49150 ± 2675	0.0026	113.3 ± 8	146.5 ± 10.7	33.2	1.3
F18L	22788 ± 1848	27677 ± 2429	0.0301	79.6 ± 3.7	97.1 ± 6.6	17.5	1.2
A20G	8349 ± 475	10555 ± 783	0.0067	30.2 ± 1.5	37.4 ± 2.4	7.2	1.3
L21H	17203 ± 1913	23891 ± 2271	0.0158	47.2 ± 4.5	66.1 ± 5.8	19.0	1.4
V22A	15790 ± 1037	22194 ± 2010	0.0077	43.9 ± 2.5	61.2 ± 5.1	17.3	1.4
V22F	29970 ± 2021	36745 ± 2458	0.0339	83.5 ± 4.6	102.5 ± 5.7	19.0	1.2
V22I	27969 ± 1731	43104 ± 3250	0.0003	75.7 ± 4.1	116.4 ± 8.5	40.7	1.5
V22L	27041 ± 1471	38357 ± 3293	0.0083	74.7 ± 3.6	105.8 ± 8.9	31.1	1.4
S23P	28512 ± 2197	38609 ± 2917	0.0067	88.2 ± 3.5	119.1 ± 5.7	31.0	1.4
S23T	32295 ± 2128	40230 ± 2181	0.0057	90.2 ± 5.1	112.8 ± 5.4	22.6	1.3
W24S	13019 ± 845	18420 ± 1212	0.0001	40 ± 2.5	56.7 ± 4	16.7	1.4
D25H	30857 ± 1142	37503 ± 1794	0.0053	94.9 ± 3.9	115.8 ± 6.5	20.9	1.2
I26N	32979 ± 2494	44191 ± 5046	0.0382	75.5 ± 4.2	97.3 ± 7.3	21.8	1.3
P27A	19346 ± 1192	27202 ± 1150	0.0001	51.9 ± 3.2	72.6 ± 2.3	20.7	1.4
P27L	26913 ± 1947	32775 ± 1415	0.0030	72.4 ± 5.4	90 ± 5.3	17.6	1.2
P27S	28366 ± 1590	38366 ± 1767	0.0003	70.4 ± 3.3	95.3 ± 3.6	24.9	1.4
P27T	26456 ± 954	34628 ± 1113	0.0001	62.4 ± 2.4	81.9 ± 3.2	19.5	1.3
G28E	27350 ± 1663	34034 ± 2028	0.0024	73.8 ± 4.5	91.1 ± 4.6	17.2	1.2
G28R	26315 ± 1950	32315 ± 1988	0.0062	71.5 ± 5.7	87.6 ± 5.4	16.1	1.2
G28W	27378 ± 1600	36559 ± 1783	0.0003	74 ± 4.4	97.9 ± 4.2	23.9	1.3
A29G	15101 ± 1719	18785 ± 1854	0.0147	44.5 ± 4.2	55.1 ± 4.4	10.6	1.2
A29P	4738 ± 402	6987 ± 388	0.0003	14 ± 1	20.6 ± 0.6	6.6	1.5
A29V	18656 ± 1649	22884 ±	0.0382	55.7 ± 4.3	68.2 ± 4.4	12.5	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1713					
R30G	21934 ± 2016	27320 ± 1888	0.0053	65.4 ± 5.2	80.7 ± 4	15.3	1.3
L32M	23345 ± 1826	30767 ± 2014	0.0067	66.9 ± 3.8	89.4 ± 4.5	22.5	1.3
L32Q	228 ± 24	5733 ± 357	0.0001	0.7 ± 0.1	16.9 ± 1.1	16.2	25.2
L32R	15594 ± 1339	24030 ± 1883	0.0033	45.4 ± 3.9	70.6 ± 5.6	25.2	1.5
L32V	17391 ± 1265	25028 ± 1678	0.0018	51.2 ± 3.7	73.7 ± 4.7	22.5	1.4
D33A	21613 ± 1926	37153 ± 2439	0.0001	55.1 ± 3.5	94.5 ± 3.5	39.4	1.7
D33E	32178 ± 2816	44926 ± 3037	0.0010	81.8 ± 5.9	116.8 ± 7.1	34.9	1.4
D33V	8815 ± 815	28371 ± 2762	0.0001	22.3 ± 1.7	71 ± 4.2	48.7	3.2
L36M	29476 ± 1787	37839 ± 2103	0.0030	75.8 ± 4.5	97.4 ± 5.7	21.6	1.3
L36V	32854 ± 2003	45155 ± 2152	0.0001	87.7 ± 8.1	118.1 ± 7.7	30.4	1.4
A37E	17508 ± 1781	22216 ± 922	0.0039	51.1 ± 3.2	68.6 ± 3.1	17.5	1.3
A37G	20059 ± 1634	26374 ± 1068	0.0011	59.5 ± 3.1	81.2 ± 3.3	21.7	1.3
A37S	28548 ± 1621	36678 ± 2507	0.0090	68.2 ± 2.9	87.8 ± 5.4	19.6	1.3
R38G	20871 ± 1596	26474 ± 1182	0.0017	59.2 ± 3.2	76.8 ± 3.1	17.5	1.3
R38M	27519 ± 2289	33201 ± 1837	0.0104	82.2 ± 4.6	105.3 ± 8.7	23.2	1.2
R38W	13728 ± 1660	19031 ± 797	0.0026	39.4 ± 3.1	58.3 ± 2	18.9	1.4
T39A	14133 ± 599	22863 ± 1308	0.0001	58 ± 2.5	92.9 ± 4.5	35.0	1.6
T39K	14243 ± 982	19261 ± 1065	0.0010	57.9 ± 3.6	78 ± 3.4	20.1	1.4
T39M	18868 ± 1035	29341 ± 1094	0.0001	42.9 ± 2.6	66.7 ± 3.3	23.8	1.6
T39R	16386 ± 946	19594 ± 1257	0.0049	66.6 ± 3.3	79.3 ± 4.2	12.7	1.2
T39S	22746 ± 1704	30290 ± 1697	0.0010	68.8 ± 3.9	98.5 ± 10.1	29.6	1.3
T41A	23027 ± 1729	35730 ± 2325	0.0001	93.8 ± 6.4	144.3 ± 7.5	50.5	1.6
T41N	15106 ± 1455	27001 ±	0.0001	61.7 ± 5.7	109.4 ± 6.3	47.7	1.8

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1828					
T41S	36978 ± 1637	47987 ± 2574	0.0001	83 ± 3.1	108.3 ± 5.2	25.2	1.3
G43A	547 ± 39	9152 ± 903	0.0001	2.1 ± 0.2	35.6 ± 4.2	33.6	16.7
L45M	10167 ± 738	15884 ± 1038	0.0001	35.4 ± 3.2	55.3 ± 4.8	20.0	1.6
L45V	7728 ± 553	12995 ± 870	0.0001	27 ± 2.4	45.5 ± 4.1	18.5	1.7
H46D	5064 ± 346	12824 ± 844	0.0001	17.5 ± 1.4	44.8 ± 3.9	27.3	2.5
H46N	4890 ± 293	16015 ± 971	0.0001	16.9 ± 1.3	55.9 ± 4.6	39.0	3.3
H46Q	5784 ± 357	12138 ± 771	0.0001	20 ± 1.5	42.4 ± 3.6	22.4	2.1
E48A	1795 ± 172	7438 ± 547	0.0001	7.4 ± 1	29.1 ± 2.7	21.7	4.1
F50Y	756 ± 43	15051 ± 1103	0.0001	2.4 ± 0.2	46.3 ± 4.9	43.9	19.9
M51R	14619 ± 996	18178 ± 722	0.0039	53.3 ± 4	65.5 ± 2.8	12.1	1.2
M51T	9539 ± 615	17742 ± 498	0.0001	37.8 ± 2.1	71.1 ± 2.2	33.3	1.9
M51V	8888 ± 629	12943 ± 674	0.0001	34.1 ± 2.8	49.2 ± 3.1	15.1	1.5
N53H	4889 ± 672	10065 ± 346	0.0001	19.2 ± 2.3	40.3 ± 1.4	21.1	2.1
N53I	12636 ± 1899	20010 ± 2488	0.0006	35 ± 3	57.2 ± 3.8	22.2	1.6
N53S	15799 ± 1945	25411 ± 2907	0.0007	47.3 ± 3.7	75.3 ± 4.1	28.0	1.6
N53T	16203 ± 1515	26147 ± 2763	0.0001	49.4 ± 3.1	78.4 ± 4.1	29.0	1.6
L54H	BLD	6158 ± 377	0.0001	N/A	17.5 ± 0.8	17.5	NC
L54R	15536 ± 1823	23973 ± 743	0.0001	44.4 ± 4.6	70.1 ± 3.1	25.8	1.5
L54V	24595 ± 2022	30741 ± 1942	0.0045	69.6 ± 4	87.9 ± 4.5	18.4	1.3
D55A	16170 ± 1627	21497 ± 801	0.0010	47 ± 4.6	63.3 ± 3.4	16.3	1.3
D55E	16212 ± 1607	22237 ± 896	0.0002	47 ± 4.3	66.2 ± 4.6	19.2	1.4
D55H	9076 ± 1049	16638 ± 569	0.0001	27.3 ± 3	50.4 ± 2.9	23.1	1.8
D55Y	2268 ± 94	9956 ± 562	0.0001	7.5 ± 0.6	32.1 ± 1.9	24.5	4.4
C56W	BLD	1854 ± 140	0.0001	N/A	5.6 ± 0.4	5.6	NC
E58K	11757 ± 839	18105 ± 1138	0.0001	37.2 ± 2.7	57.6 ± 4.2	20.5	1.5
E59A	17204 ± 1538	21575 ± 1115	0.0014	47 ± 3.9	58.9 ± 2.2	11.9	1.3
E59D	22266 ± 1484	28238 ± 1077	0.0005	69.7 ± 3.8	89.5 ± 3.5	19.8	1.3
E59G	4551 ± 506	12357 ± 924	0.0001	12.4 ± 0.9	35.1 ± 1.6	22.7	2.7
E59Q	13611 ± 1152	18673 ±	0.0011	42.7 ± 3.2	58.8 ± 3.9	16.0	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1404					
E59V	2072 ± 168	7546 ± 732	0.0001	6.7 ± 0.6	24.4 ± 2.8	17.8	3.6
P60A	19972 ± 1596	26820 ± 1669	0.0006	54.9 ± 4	73.2 ± 3	18.3	1.3
P60Q	15470 ± 799	26238 ± 1132	0.0001	48.7 ± 2	82.7 ± 2.9	34.0	1.7
P60R	10622 ± 882	17095 ± 698	0.0001	30 ± 2.1	48.8 ± 2	18.8	1.6
D61E	29588 ± 1345	37109 ± 2077	0.0049	97.9 ± 6	119.2 ± 5	21.4	1.3
D61V	15741 ± 668	21299 ± 748	0.0001	54.8 ± 2.9	74.8 ± 3.9	20.0	1.4
S62A	31726 ± 1779	38602 ± 2163	0.0030	95.2 ± 3.8	115.5 ± 4.2	20.2	1.2
S62C	12299 ± 669	16978 ± 1074	0.0006	41.3 ± 1.9	58.2 ± 4.6	16.9	1.4
S62F	10360 ± 706	15534 ± 903	0.0002	34.5 ± 1.7	52.6 ± 3	18.1	1.5
S62P	245 ± 39	6945 ± 844	0.0001	0.7 ± 0.1	19.3 ± 1.6	18.6	28.3
S62Y	12108 ± 1047	19476 ± 875	0.0001	40 ± 2.4	66.7 ± 3.7	26.7	1.6
I64L	229 ± 32	8452 ± 484	0.0001	0.7 ± 0.1	24.3 ± 1.2	23.6	36.9
I64V	18259 ± 1030	27706 ± 637	0.0001	54.5 ± 3.2	82.7 ± 2.6	28.2	1.5
S65C	26986 ± 2021	35417 ± 2097	0.0022	61.1 ± 2.3	81 ± 1.9	19.9	1.3
S65G	19996 ± 2296	33127 ± 2448	0.0005	64 ± 7.4	105.3 ± 7.1	41.3	1.7
S65R	37555 ± 2042	45657 ± 2084	0.0053	87.1 ± 4	105.7 ± 2.4	18.5	1.2
E66D	24426 ± 1399	30874 ± 1190	0.0007	56.4 ± 2	72.2 ± 2.3	15.8	1.3
E66V	10943 ± 1124	15435 ± 1251	0.0007	24.7 ± 1.7	35.2 ± 1.7	10.5	1.4
K67E	30290 ± 1420	46106 ± 1265	0.0001	70.7 ± 2.7	108.2 ± 2.8	37.6	1.5
K67M	22374 ± 1366	33812 ± 1237	0.0001	53.3 ± 2.9	81.1 ± 2.6	27.8	1.5
K67N	30951 ± 2447	48271 ± 1855	0.0001	73.9 ± 5.6	115.9 ± 4.1	42.0	1.6
K67Q	33571 ± 1439	48101 ± 1363	0.0001	78.2 ± 2.3	113.2 ± 3.4	35.0	1.4
K67T	29063 ± 2114	42744 ± 1271	0.0001	69.3 ± 4.9	102.5 ± 2.6	33.2	1.5
L68I	1191 ± 125	9012 ± 534	0.0001	2.8 ± 0.3	21.5 ± 1.1	18.7	7.6
F69I	376 ± 38	10829 ± 488	0.0001	0.9 ± 0.1	25.4 ± 0.8	24.5	28.8
F69Y	1500 ± 119	18806 ±	0.0001	3.3 ± 0.2	40.7 ± 2.2	37.4	12.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1141					
M70I	24534 ± 1064	32895 ± 1518	0.0001	60.7 ± 2.7	82.2 ± 4.6	21.5	1.3
M70K	25582 ± 1732	38457 ± 1757	0.0001	62.5 ± 3	94.9 ± 4.1	32.5	1.5
M70L	26515 ± 1172	31930 ± 1211	0.0024	63.9 ± 1.4	78.4 ± 3.4	14.5	1.2
M70R	27578 ± 2110	42595 ± 1951	0.0001	59.4 ± 4	93 ± 5	33.6	1.5
E71A	23766 ± 1537	32700 ± 1312	0.0001	59.3 ± 4.5	81.1 ± 3.6	21.8	1.4
E71D	26962 ± 1987	36176 ± 2174	0.0009	61.1 ± 2.5	82.7 ± 3.1	21.7	1.3
E71G	22820 ± 1979	32128 ± 878	0.0001	54.7 ± 3	80.3 ± 3.4	25.6	1.4
E71Q	29109 ± 1574	37795 ± 1474	0.0003	70.8 ± 2.4	93.3 ± 3.4	22.5	1.3
E71V	25328 ± 994	33957 ± 879	0.0001	62.8 ± 2.8	85.3 ± 3.8	22.4	1.3
M72L	8208 ± 664	23988 ± 1422	0.0001	18.5 ± 1.1	54.9 ± 2.1	36.4	2.9
M72T	25205 ± 1791	32476 ± 2471	0.0206	57 ± 2.4	73.4 ± 3.3	16.5	1.3
A73S	23566 ± 1631	31993 ± 1944	0.0033	53.7 ± 2.9	73.3 ± 3	19.6	1.4
A73T	23379 ± 1999	28403 ± 1642	0.0283	53.6 ± 3.3	66 ± 2.2	12.4	1.2
E74D	28411 ± 1782	39202 ± 2134	0.0003	69.6 ± 2.7	96.8 ± 2.7	27.2	1.4
E74G	23718 ± 1447	33068 ± 1675	0.0002	58.8 ± 2.8	82.9 ± 3.5	24.2	1.4
E74K	23026 ± 2084	27539 ± 1592	0.0193	52.4 ± 4.3	63.1 ± 2.4	10.6	1.2
E74V	20975 ± 1489	25386 ± 1823	0.0234	51.6 ± 3.1	63.2 ± 4.1	11.6	1.2
L75F	25253 ± 1313	30602 ± 1493	0.0042	63.5 ± 3.6	76.7 ± 3.1	13.3	1.2
L75P	4084 ± 434	5513 ± 287	0.0111	9.7 ± 0.9	13.6 ± 1	3.9	1.4
M76V	11543 ± 644	20077 ± 1484	0.0001	30 ± 1.2	51.3 ± 2.6	21.3	1.7
V77I	29128 ± 1593	36588 ± 2669	0.0360	72 ± 3.8	87.4 ± 2.9	15.4	1.3
V77L	29482 ± 1970	35834 ± 1940	0.0174	77 ± 5.5	92.8 ± 3.2	15.7	1.2
S78L	27575 ± 1856	34892 ±	0.0024	68.9 ± 2.5	89.4 ± 3.2	20.5	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1683					
S78P	2263 ± 319	3971 ± 333	0.0014	5.4 ± 0.7	9.7 ± 0.5	4.3	1.8
E79A	24732 ± 1717	33721 ± 1802	0.0011	72 ± 4.8	100.2 ± 6.9	28.3	1.4
E79D	38422 ± 3185	51309 ± 3083	0.0008	112.5 ± 9.3	153.4 ± 11.9	40.8	1.3
E79G	23729 ± 2129	34762 ± 2171	0.0005	68.9 ± 5.6	104.1 ± 8.5	35.2	1.5
E79K	12002 ± 931	19360 ± 953	0.0001	29.9 ± 1.3	50.5 ± 3	20.6	1.6
E79Q	31940 ± 2387	44470 ± 3000	0.0007	92.6 ± 6.2	134 ± 11.8	41.4	1.4
E79V	3360 ± 551	8915 ± 565	0.0001	9.8 ± 1.5	26.3 ± 1.9	16.6	2.7
G80A	12723 ± 1236	21243 ± 1698	0.0001	35.3 ± 3.2	60.7 ± 5.7	25.4	1.7
G80C	4279 ± 732	8085 ± 487	0.0005	12.5 ± 2	24 ± 1.6	11.5	1.9
G80S	14825 ± 1175	24788 ± 1376	0.0001	43.2 ± 3.3	73.8 ± 5.1	30.6	1.7
W81L	BLD	1190 ± 99	0.0001	N/A	4.4 ± 0.3	4.4	NC
K82E	7610 ± 608	10952 ± 967	0.0100	30.7 ± 2.3	43.7 ± 3.2	12.9	1.4
K82M	19592 ± 1306	25993 ± 2122	0.0266	72.6 ± 4	94.8 ± 5.2	22.3	1.3
K82N	11724 ± 855	17397 ± 1132	0.0005	43.5 ± 2.6	63.9 ± 2.5	20.4	1.5
K82R	22252 ± 1312	27326 ± 1986	0.0455	83.6 ± 4.2	101.4 ± 5.6	17.7	1.2
K82T	13117 ± 769	17594 ± 1185	0.0026	49.2 ± 2.4	65.5 ± 3.5	16.3	1.3
D83A	19999 ± 1698	24545 ± 1346	0.0067	65.6 ± 3.9	81 ± 2.6	15.4	1.2
D83E	26423 ± 1478	41691 ± 3309	0.0007	76.3 ± 3.5	120.2 ± 9	43.9	1.6
D83G	16734 ± 1241	21951 ± 1455	0.0049	54.7 ± 2.5	72 ± 3	17.3	1.3
D83V	14758 ± 1130	25238 ± 1768	0.0001	45.8 ± 2.2	78.5 ± 3.9	32.7	1.7
A84E	9978 ± 952	16862 ± 1319	0.0003	27.7 ± 1.8	48.6 ± 3.9	20.9	1.7
A84G	9870 ± 942	18181 ± 1377	0.0001	28.6 ± 2.3	52.4 ± 3.3	23.9	1.8
A84P	180 ± 47	1255 ± 141	0.0001	0.6 ± 0.2	3.9 ± 0.4	3.3	7.0
A84S	27798 ± 2763	36913 ± 2263	0.0042	84.8 ± 5	116.1 ± 5.6	31.3	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
A84T	16960 ± 1350	23585 ± 2022	0.0072	48.8 ± 2.7	69.3 ± 6	20.5	1.4
A84V	34751 ± 2600	41833 ± 2901	0.0455	94.9 ± 4.5	115.4 ± 6	20.5	1.2
G85A	3114 ± 442	8107 ± 550	0.0001	7.9 ± 0.9	20.8 ± 1.2	12.9	2.6
G85C	926 ± 66	3079 ± 427	0.0001	2.4 ± 0.2	7.5 ± 0.8	5.1	3.3
G85R	9145 ± 1128	13622 ± 1053	0.0039	22.5 ± 2.2	33.7 ± 1.5	11.2	1.5
Y86F	12275 ± 707	16114 ± 468	0.0002	31 ± 1.7	41 ± 1.7	10.0	1.3
E87G	16130 ± 877	20394 ± 867	0.0008	41 ± 2.6	52 ± 3	11.0	1.3
Y88H	11199 ± 689	16074 ± 612	0.0001	28.4 ± 1.3	41.5 ± 1.6	13.1	1.4
Y88N	5381 ± 557	7561 ± 298	0.0001	13.5 ± 1.1	19.5 ± 0.9	6.0	1.4
L89V	26558 ± 1501	33849 ± 1243	0.0005	63.4 ± 4.6	80.7 ± 4.4	17.3	1.3
I91F	353 ± 36	3846 ± 338	0.0001	1 ± 0.1	9.7 ± 0.5	8.7	10.9
I91L	17057 ± 1308	28279 ± 1631	0.0001	54.3 ± 6	91.4 ± 9.9	37.0	1.7
I91M	19360 ± 1837	32190 ± 1335	0.0001	47.9 ± 3.4	82.4 ± 3.8	34.5	1.7
I91S	946 ± 38	3966 ± 176	0.0001	2.5 ± 0.2	10.2 ± 0.6	7.7	4.2
M96L	24584 ± 1414	37462 ± 1866	0.0001	61.8 ± 2.8	93.8 ± 3.1	32.0	1.5
M96T	12103 ± 1633	18415 ± 1827	0.0033	30.3 ± 3.3	46.7 ± 3.4	16.4	1.5
A97D	17634 ± 1789	29319 ± 4081	0.0039	45 ± 3.4	74.5 ± 9.5	29.5	1.7
A97S	21262 ± 1383	27841 ± 2335	0.0128	55.7 ± 3.7	70.9 ± 4.2	15.1	1.3
A97T	11157 ± 776	19875 ± 1502	0.0001	29.4 ± 2.2	50.9 ± 2.7	21.4	1.8
P98H	21896 ± 1232	29920 ± 1808	0.0013	60.8 ± 3.1	83.4 ± 4.6	22.5	1.4
P98L	24223 ± 1555	31835 ± 2399	0.0072	69 ± 5.5	88.5 ± 6.3	19.6	1.3
P98R	24969 ± 1730	31289 ± 2550	0.0405	69.4 ± 4	85.8 ± 5.8	16.4	1.3
Q99E	25264 ± 1668	34635 ± 3117	0.0104	70.3 ± 4.1	95.8 ± 7.9	25.5	1.4
Q99L	23382 ± 1548	33479 ± 2746	0.0012	65.9 ± 5.1	93.4 ± 7.3	27.4	1.4
Q99P	3034 ± 340	9885 ± 794	0.0001	8.8 ± 1.2	28 ± 2.4	19.1	3.3
Q99R	32963 ± 1757	41024 ±	0.0193	93.4 ± 6.3	114.8 ± 8	21.4	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		3001					
D101A	10144 ± 1069	14707 ± 1289	0.0049	23.9 ± 3	34.1 ± 3.3	10.2	1.5
D101E	10465 ± 624	14682 ± 993	0.0010	23.9 ± 1.6	34 ± 2.8	10.1	1.4
D101G	18091 ± 1103	23672 ± 1428	0.0033	41.8 ± 3.1	54.5 ± 3.8	12.7	1.3
D101H	7311 ± 556	10493 ± 561	0.0002	16.5 ± 1.2	23.8 ± 1.3	7.3	1.4
D101V	3368 ± 179	7489 ± 936	0.0001	7.8 ± 0.5	18 ± 2.6	10.2	2.2
S102A	17330 ± 2084	26790 ± 1958	0.0018	42.6 ± 3.5	69.9 ± 5.1	27.3	1.6
S102P	27252 ± 1778	35885 ± 2754	0.0111	69.4 ± 3.4	91.7 ± 5	22.3	1.3
S102T	22123 ± 2319	29662 ± 2559	0.0339	56.4 ± 5.2	76.9 ± 6.2	20.5	1.3
G104A	5271 ± 397	19670 ± 1202	0.0001	14.8 ± 1	55.2 ± 3	40.4	3.7
G104D	14123 ± 1096	24797 ± 1771	0.0001	39.3 ± 2.6	69.8 ± 4.7	30.5	1.8
G104S	5720 ± 464	22242 ± 1000	0.0001	17.9 ± 1.8	69.8 ± 5.8	52.0	3.9
R105G	16513 ± 681	22993 ± 1042	0.0001	38 ± 2.1	53.3 ± 3.5	15.3	1.4
R105I	9696 ± 798	12128 ± 1157	0.0158	33.4 ± 2.2	41.6 ± 3.1	8.2	1.3
R105K	25495 ± 1793	31647 ± 2251	0.0360	76.2 ± 2.9	96.7 ± 5.2	20.5	1.2
R105T	12553 ± 603	17062 ± 1134	0.0020	44 ± 2.2	59.6 ± 3.9	15.6	1.4
L106H	856 ± 58	3009 ± 399	0.0001	3 ± 0.2	10.2 ± 1.1	7.3	3.5
L106I	13485 ± 1014	20120 ± 1416	0.0002	46.4 ± 2.7	70 ± 4.7	23.6	1.5
L106P	8835 ± 878	16075 ± 1039	0.0001	30.7 ± 2.7	56.5 ± 3.9	25.8	1.8
L106V	15393 ± 1288	20991 ± 1611	0.0033	53.6 ± 4.3	73.4 ± 5.9	19.8	1.4
Q107E	13148 ± 985	16149 ± 1059	0.0111	45.7 ± 3.1	56.2 ± 3.3	10.4	1.2
Q107H	12307 ± 487	14822 ± 384	0.0001	41.7 ± 1.5	50.8 ± 2	9.1	1.2
Q107K	14579 ± 2689	20402 ± 3399	0.0128	38.2 ± 3.9	54.6 ± 4.8	16.4	1.4
A108E	11629 ± 835	15648 ± 1305	0.0111	38.4 ± 2.6	52.6 ± 4.6	14.2	1.4
A108V	4914 ± 799	17249 ±	0.0001	13.3 ± 1.7	47.7 ± 4.6	34.4	3.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2284					
D109A	6345 ± 1034	13742 ± 1780	0.0002	17.5 ± 2.2	38 ± 3.7	20.4	2.2
D109E	13839 ± 1179	16926 ± 1156	0.0147	41.3 ± 3.4	50.6 ± 3.6	9.3	1.2
D109H	7540 ± 684	16483 ± 1317	0.0001	24.6 ± 1.7	54.6 ± 3.5	30.0	2.2
D109N	1475 ± 83	12358 ± 973	0.0001	5 ± 0.3	41.5 ± 2.8	36.5	8.4
D109Y	212 ± 30	2530 ± 415	0.0001	0.7 ± 0.1	8.2 ± 1.1	7.5	11.9
P110T	20474 ± 1528	26745 ± 1678	0.0049	62.6 ± 5.9	81.2 ± 6.5	18.6	1.3
F113V	341 ± 41	3614 ± 596	0.0001	1.1 ± 0.1	10.3 ± 1	9.2	10.6
F113Y	BLD	1328 ± 79	0.0001	N/A	4.4 ± 0.3	4.4	NC
P114L	6229 ± 901	7973 ± 626	0.0062	18.3 ± 2.1	23.7 ± 1.3	5.4	1.3
H115D	10284 ± 1141	15258 ± 1412	0.0028	30.7 ± 2.9	44.8 ± 3	14.1	1.5
H115N	13745 ± 890	23018 ± 1098	0.0001	44.9 ± 2.5	75 ± 2.5	30.1	1.7
G116R	1922 ± 143	5251 ± 464	0.0001	5.4 ± 0.3	15.4 ± 1.5	9.9	2.7
I117M	20226 ± 1373	31280 ± 1153	0.0001	54.2 ± 3.9	83.5 ± 3.6	29.4	1.6
I117T	1607 ± 54	3303 ± 308	0.0001	4.3 ± 0.2	9 ± 0.9	4.7	2.1
A121V	7301 ± 253	26639 ± 1124	0.0001	21.5 ± 1.2	78.2 ± 4.2	56.7	3.7
Y123D	15093 ± 815	18723 ± 1237	0.0083	43.4 ± 1.6	53.6 ± 2.7	10.2	1.2
Y123F	22066 ± 1408	33544 ± 1384	0.0001	63.6 ± 3.3	97.4 ± 3.4	33.8	1.5
Y123N	13817 ± 816	20466 ± 846	0.0001	40.9 ± 3.2	60.6 ± 4.1	19.7	1.5
Y123S	14556 ± 986	21255 ± 1484	0.0008	41.7 ± 2.1	61 ± 3.6	19.3	1.5
V124I	32074 ± 1858	43288 ± 2179	0.0003	80.7 ± 2	111.3 ± 4.5	30.6	1.4
H125D	995 ± 106	3282 ± 375	0.0001	2.3 ± 0.2	8.8 ± 1.4	6.5	3.3
H125N	14162 ± 994	20228 ± 1240	0.0006	33.5 ± 1.8	48.4 ± 2.7	14.9	1.4
H125R	14738 ± 699	24004 ± 987	0.0001	36 ± 1.2	59.1 ± 1.9	23.0	1.6
S126C	7046 ± 488	10050 ± 554	0.0004	16.9 ± 1.1	24.5 ± 1.5	7.5	1.4
S126I	28685 ± 1923	35340 ± 2027	0.0234	69.8 ± 5.1	85.9 ± 5.3	16.0	1.2
K127E	8968 ± 519	11003 ± 768	0.0147	25.8 ± 1.1	32.2 ± 2.3	6.4	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
G128A	8484 ± 872	10204 ± 703	0.0319	20.8 ± 2	25.9 ± 2.3	5.1	1.2
L129V	12614 ± 1265	19488 ± 1603	0.0012	31.8 ± 3.3	48.1 ± 4.5	16.4	1.5
K130M	12335 ± 890	16496 ± 921	0.0020	30.5 ± 2.1	41.4 ± 2.6	10.9	1.3
K130N	8597 ± 678	12595 ± 989	0.0017	21.5 ± 1.9	31.5 ± 3	10.1	1.5
K130Q	11880 ± 450	16001 ± 701	0.0001	35.8 ± 2.6	47.8 ± 3.1	12.0	1.4
L131V	18644 ± 1664	24913 ± 3151	0.0319	40.5 ± 2.8	53.2 ± 5.3	12.7	1.3
I133L	24431 ± 1181	31550 ± 1420	0.0004	60.7 ± 2.7	78.2 ± 3.1	17.5	1.3
I133T	4362 ± 397	10255 ± 335	0.0001	10.8 ± 1	25.8 ± 1.1	15.0	2.4
I133V	38738 ± 1624	47299 ± 1885	0.0007	96.2 ± 3.7	118.1 ± 5.1	21.9	1.2
A135E	10143 ± 752	12954 ± 678	0.0045	25.1 ± 1.5	32.5 ± 1.6	7.4	1.3
A135G	29959 ± 2193	36552 ± 2309	0.0206	73.9 ± 3.8	90 ± 3.6	16.1	1.2
A135S	16777 ± 897	21383 ± 1125	0.0020	45.6 ± 2.9	57.9 ± 3.2	12.2	1.3
A135T	7906 ± 694	18890 ± 2092	0.0001	17.4 ± 1.3	40.5 ± 3.4	23.2	2.4
D136A	8054 ± 482	12166 ± 927	0.0001	20.4 ± 1.1	29.8 ± 1	9.4	1.5
D136N	5079 ± 248	9827 ± 630	0.0001	13 ± 0.8	24.2 ± 0.9	11.2	1.9
D136V	17164 ± 1203	47647 ± 3779	0.0001	42.2 ± 1.7	116.4 ± 5.5	74.2	2.8
V137A	22393 ± 1429	40016 ± 2785	0.0001	61.1 ± 4.6	106.6 ± 5.9	45.4	1.8
V137D	516 ± 80	4757 ± 618	0.0001	1.4 ± 0.2	13 ± 1.6	11.6	9.2
V137G	16515 ± 1170	36258 ± 1701	0.0001	45.9 ± 4.2	98.2 ± 5	52.4	2.2
V137I	12148 ± 597	21313 ± 987	0.0001	32.8 ± 1.6	57.4 ± 2.5	24.7	1.8
V137L	15359 ± 656	19794 ± 1475	0.0045	41.6 ± 2.1	53.3 ± 3.7	11.7	1.3
G138A	4768 ± 480	11112 ± 732	0.0001	14.4 ± 1.1	34.5 ± 1.5	20.1	2.3
N139H	29115 ± 2336	40678 ± 3158	0.0024	73.1 ± 5.4	101.2 ± 7.1	28.1	1.4
N139I	17180 ± 1455	26326 ± 1627	0.0001	51.8 ± 5.1	78.3 ± 4.5	26.4	1.5
N139K	33797 ± 2244	45090 ± 2667	0.0022	93.6 ± 5.8	127.4 ± 8.8	33.8	1.3
N139Y	19998 ± 1682	24303 ± 2079	0.0405	52.3 ± 3.8	64 ± 5.2	11.7	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
K140E	26053 ± 1925	46670 ± 2685	0.0001	72.6 ± 5.8	132.1 ± 9	59.5	1.8
K140I	15415 ± 1294	32440 ± 2092	0.0001	42.7 ± 3.3	92.1 ± 7.1	49.4	2.1
K140N	40575 ± 2928	54681 ± 3030	0.0013	113.8 ± 9.5	154.1 ± 11.1	40.3	1.4
K140Q	42995 ± 3236	59162 ± 3600	0.0009	123.2 ± 12.1	165.7 ± 9.7	42.5	1.4
K140R	50348 ± 3558	62820 ± 3401	0.0120	141.5 ± 12	180.9 ± 15	39.4	1.3
T141S	22602 ± 2254	34806 ± 2770	0.0018	63.8 ± 7.1	98.2 ± 9.1	34.4	1.5
A143E	7681 ± 439	11458 ± 884	0.0015	25.9 ± 1.5	37.3 ± 1.8	11.4	1.5
A143G	20419 ± 1260	36821 ± 2997	0.0001	67.8 ± 3.4	119.7 ± 5.9	51.9	1.8
G144A	20304 ± 1590	27268 ± 1039	0.0011	44.9 ± 3.6	60.4 ± 2.8	15.5	1.3
G144C	759 ± 69	2988 ± 262	0.0001	2.5 ± 0.2	9.5 ± 0.8	7.1	3.9
G144R	10574 ± 838	21406 ± 1764	0.0001	35.7 ± 2.8	73.4 ± 6.5	37.7	2.0
G144S	14190 ± 967	23153 ± 1847	0.0003	47.6 ± 2.4	78 ± 5.6	30.4	1.6
F145C	768 ± 54	11083 ± 678	0.0001	2.1 ± 0.2	27.8 ± 0.8	25.7	14.4
F145L	5455 ± 412	29794 ± 1799	0.0001	13.9 ± 0.8	75.7 ± 2.9	61.8	5.5
F145V	BLD	2359 ± 333	0.0001	N/A	5.7 ± 0.6	5.7	NC
F145Y	41985 ± 2942	51524 ± 2970	0.0147	108.1 ± 6.2	131.7 ± 5.1	23.5	1.2
P146A	15393 ± 1271	25029 ± 1628	0.0002	38.7 ± 2.5	64.1 ± 4.4	25.4	1.6
P146H	3220 ± 211	11903 ± 844	0.0001	8.5 ± 0.7	30.2 ± 2.1	21.8	3.7
P146L	9940 ± 899	14540 ± 903	0.0009	24.7 ± 1.8	37.1 ± 2.2	12.4	1.5
P146T	13711 ± 1154	24123 ± 2081	0.0004	33.6 ± 1.5	58.6 ± 2.4	25.0	1.8
G147A	BLD	1159 ± 74	0.0001	N/A	3 ± 0.2	3.0	NC
S148C	11927 ± 1020	19343 ± 919	0.0001	30.2 ± 2.2	49.5 ± 2	19.3	1.6
S148G	435 ± 55	4879 ± 263	0.0001	1.1 ± 0.1	12.9 ± 1	11.8	11.2
S148T	24827 ± 1221	30620 ± 813	0.0006	66.5 ± 3.8	82.4 ± 3.7	15.9	1.2
F149C	15198 ± 1188	19032 ± 1272	0.0301	47 ± 4.4	60.9 ± 6.4	13.9	1.3
G150E	18804 ± 1070	22710 ± 1059	0.0120	61.5 ± 6.6	73.8 ± 7	12.3	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
G150V	1080 ± 63	4639 ± 361	0.0001	2.9 ± 0.1	12.1 ± 0.7	9.2	4.3
Y151C	11271 ± 579	15859 ± 752	0.0001	32.4 ± 1.5	45.6 ± 2	13.2	1.4
Y151D	10673 ± 604	15196 ± 1025	0.0006	29.3 ± 1.7	40.8 ± 2.2	11.5	1.4
Y151S	30047 ± 1943	37527 ± 2003	0.0067	84.8 ± 4.2	107 ± 4.9	22.2	1.3
Y152F	18675 ± 907	23612 ± 1095	0.0013	45.4 ± 2.6	56.8 ± 2.7	11.4	1.3
Y152S	9917 ± 917	16642 ± 1218	0.0002	27.1 ± 1.7	46.7 ± 2.6	19.6	1.7
D153A	22606 ± 1445	30854 ± 1997	0.0028	60.1 ± 2.4	81.6 ± 2.3	21.6	1.4
D153H	23578 ± 1741	31052 ± 1774	0.0030	60.5 ± 2.2	81 ± 2.1	20.5	1.3
D153N	29386 ± 1518	39338 ± 1551	0.0001	65.6 ± 2.8	89.7 ± 4.4	24.1	1.3
D153V	7357 ± 1139	16301 ± 766	0.0001	17.4 ± 2	42.4 ± 1.6	25.0	2.2
D153Y	12609 ± 1299	22535 ± 1174	0.0001	29.1 ± 3.1	52.4 ± 2.8	23.3	1.8
A156G	17406 ± 1187	23415 ± 1710	0.0033	46.7 ± 2.7	63.6 ± 4.3	16.9	1.4
Q157E	28269 ± 1306	37204 ± 2126	0.0007	77.4 ± 4.1	101.5 ± 6.1	24.1	1.3
Q157K	9815 ± 1083	31331 ± 2428	0.0001	24.1 ± 1.8	79.7 ± 5	55.6	3.2
Q157L	5734 ± 700	28942 ± 2013	0.0001	14.3 ± 1.5	74.4 ± 4.3	60.2	5.1
Q157P	3887 ± 487	20888 ± 1527	0.0001	9 ± 1	49.6 ± 3.4	40.6	5.4
T158A	14835 ± 1107	25678 ± 1673	0.0001	38.6 ± 2.5	67.3 ± 3.1	28.7	1.7
T158I	17360 ± 1159	24097 ± 1695	0.0042	49 ± 2.7	67.8 ± 3.4	18.8	1.4
T158N	1906 ± 106	5991 ± 499	0.0001	5.4 ± 0.2	18.2 ± 2	12.8	3.1
T158S	31043 ± 2073	39060 ± 2937	0.0169	79.3 ± 4	99.1 ± 5.6	19.8	1.3
F159I	21543 ± 1754	29402 ± 1960	0.0057	64.7 ± 3.5	89.3 ± 4.2	24.6	1.4
F159L	22840 ± 1245	31357 ± 1408	0.0001	75.6 ± 8.4	103.6 ± 10.7	28.0	1.4
F159V	16474 ± 1048	26241 ± 1907	0.0001	50.9 ± 2.9	80.7 ± 4.8	29.8	1.6
F159Y	2573 ± 301	10052 ± 825	0.0001	7.7 ± 0.7	30.1 ± 1.7	22.4	3.9

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
A160G	13634 ± 2705	19647 ± 3137	0.0017	35.1 ± 3.7	54.1 ± 5.3	19.0	1.4
A160S	18308 ± 685	27775 ± 1478	0.0001	56 ± 3.1	85.9 ± 6.3	29.9	1.5
A160T	20193 ± 1713	29082 ± 1980	0.0001	59.6 ± 3.5	90.9 ± 8.1	31.3	1.4
A160V	15511 ± 1847	22124 ± 1885	0.0013	44.1 ± 2.7	66 ± 4.8	21.9	1.4
D161H	21949 ± 2587	26457 ± 2512	0.0026	61.5 ± 2.9	77 ± 3.8	15.5	1.2
D161N	19553 ± 2838	24298 ± 3201	0.0062	54.5 ± 4.3	68.7 ± 4.9	14.1	1.2
D161V	13728 ± 1344	19117 ± 2241	0.0057	43.7 ± 1.7	59.7 ± 2.7	16.0	1.4
D161Y	11060 ± 1571	21231 ± 2136	0.0001	31 ± 2.5	63.1 ± 4.6	32.1	1.9
W162S	653 ± 38	3019 ± 210	0.0001	2.6 ± 0.2	11.8 ± 0.8	9.2	4.6
V164A	6491 ± 691	8468 ± 832	0.0147	24.5 ± 1.8	32 ± 2.2	7.5	1.3
V164I	12164 ± 1271	23219 ± 2640	0.0003	45.1 ± 3.4	87.1 ± 8.2	41.9	1.9
V164L	22055 ± 1619	36486 ± 1952	0.0001	51.2 ± 3.8	86.2 ± 5.2	35.0	1.7
D165A	271 ± 30	1397 ± 86	0.0001	1 ± 0.1	5.4 ± 0.3	4.4	5.2
D165E	1442 ± 43	6279 ± 288	0.0001	5.4 ± 0.2	23.8 ± 1.6	18.4	4.4
L166M	15603 ± 1630	27922 ± 1578	0.0001	55.2 ± 4.5	104 ± 7.3	48.8	1.8
L166Q	5656 ± 325	14720 ± 616	0.0001	18.4 ± 1.2	47.6 ± 1.9	29.2	2.6
L167I	14763 ± 942	22948 ± 1321	0.0001	46.8 ± 2.2	72.9 ± 2.7	26.1	1.6
F169C	6861 ± 977	16396 ± 1516	0.0001	18.1 ± 2	44.9 ± 2.3	26.9	2.4
F169L	15588 ± 1463	26527 ± 1806	0.0001	47.8 ± 2.9	82.3 ± 3.2	34.5	1.7
F169V	2870 ± 239	16145 ± 1680	0.0001	10.2 ± 0.9	53 ± 2.1	42.8	5.6
F169Y	14358 ± 1768	23459 ± 2391	0.0003	45.3 ± 2.8	75.5 ± 3.6	30.2	1.6
G171A	19081 ± 1801	27514 ± 2486	0.0030	57.6 ± 2.8	84 ± 5.7	26.4	1.4
G171V	856 ± 62	3111 ± 411	0.0001	2.8 ± 0.2	9.2 ± 0.9	6.4	3.6
Y173C	17669 ± 1240	27924 ± 1225	0.0001	51.1 ± 3.6	80.5 ± 3.3	29.3	1.6
Y173F	26479 ± 1523	33158 ± 657	0.0004	76.5 ± 4.2	97.7 ± 4.7	21.2	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
Y173H	21234 ± 879	27455 ± 1147	0.0002	61.9 ± 3.4	80.2 ± 4.6	18.3	1.3
Y173S	21751 ± 1625	26270 ± 994	0.0007	61.4 ± 3.3	76.2 ± 3.3	14.8	1.2
D175G	23065 ± 2315	28273 ± 1968	0.0128	74.7 ± 6.7	92.8 ± 6.2	18.1	1.2
D175H	18529 ± 1174	26201 ± 994	0.0001	60.7 ± 3.4	87.1 ± 3.9	26.4	1.4
D175V	10430 ± 915	16384 ± 1039	0.0001	33.7 ± 2.2	53.5 ± 2.5	19.7	1.6
D175Y	8991 ± 838	15923 ± 778	0.0001	29.4 ± 2.4	52.3 ± 1.9	22.9	1.8
S176C	20097 ± 1126	24777 ± 960	0.0067	63.3 ± 3.9	79.5 ± 5.1	16.2	1.2
S176R	22675 ± 886	30159 ± 1226	0.0001	66.3 ± 2	88.3 ± 3.3	22.0	1.3
L177F	15605 ± 911	28893 ± 1210	0.0001	45.3 ± 2.1	84 ± 2.3	38.7	1.9
L177M	23730 ± 946	33080 ± 829	0.0001	69.5 ± 2.3	97.4 ± 2.7	27.9	1.4
L177S	17445 ± 533	29868 ± 1909	0.0001	51.4 ± 1.7	87.2 ± 4.5	35.9	1.7
L177V	23616 ± 1282	31347 ± 1132	0.0001	68.9 ± 3.2	91.8 ± 2.8	22.9	1.3
L177W	17321 ± 1025	30075 ± 867	0.0001	50.5 ± 2.6	88.2 ± 2	37.6	1.7
E178A	23910 ± 1511	29125 ± 2326	0.0481	70.3 ± 4.9	84.8 ± 6.8	14.5	1.2
E178G	17470 ± 2323	26566 ± 4263	0.0219	43.1 ± 4.7	61.7 ± 6.4	18.6	1.5
E178K	25584 ± 1225	31222 ± 1660	0.0077	74.5 ± 3.4	90.9 ± 4.8	16.4	1.2
E178Q	23272 ± 1501	29671 ± 1733	0.0062	68.1 ± 4.5	86.4 ± 5	18.3	1.3
L180M	35987 ± 2266	47587 ± 2132	0.0002	93.4 ± 6.6	122.9 ± 5.5	29.5	1.3
L180S	5625 ± 604	18335 ± 964	0.0001	15.4 ± 1.5	50.9 ± 2.3	35.5	3.3
A181P	10948 ± 725	21274 ± 1279	0.0001	31.7 ± 2	61.5 ± 3.3	29.8	1.9
A181T	17946 ± 1002	24490 ± 1576	0.0012	52.1 ± 2.7	71.3 ± 4.6	19.2	1.4
A181V	26667 ± 1945	32358 ± 2863	0.0339	79.1 ± 3.5	93.2 ± 5.3	14.2	1.2
D182A	33673 ± 2886	44436 ± 3828	0.0096	101.5± 5.7	133.3 ± 8.2	31.8	1.3
D182E	28082 ± 2023	38956 ± 2806	0.0011	84.8 ± 4	117.1 ± 4.5	32.3	1.4
D182V	26881 ± 2166	42107 ± 3524	0.0005	80.2 ± 4.2	124.8 ± 6.9	44.7	1.6

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
D182Y	28377 ± 2226	39247 ± 3250	0.0062	84.7 ± 4.1	116.5 ± 6.4	31.9	1.4
Y184F	26088 ± 1334	36815 ± 2009	0.0002	77.9 ± 4.4	109.7 ± 5.8	31.8	1.4
Y184H	10980 ± 867	17894 ± 1145	0.0001	30.2 ± 2.9	48.6 ± 3.5	18.4	1.6
Y184S	5213 ± 371	13965 ± 799	0.0001	15.4 ± 1	40.6 ± 1.6	25.2	2.7
K185 M	33484 ± 2151	44387 ± 2696	0.0014	75.1 ± 4.6	102.9 ± 9	27.8	1.3
K185N	833 ± 38	10540 ± 618	0.0001	1.9 ± 0.1	24.4 ± 1.9	22.5	12.7
K185Q	14992 ± 947	25543 ± 1463	0.0001	43.6 ± 2.2	74.5 ± 2.9	30.9	1.7
K185T	32028 ± 1167	39805 ± 2259	0.0024	73.6 ± 4.4	92.6 ± 7.8	19.0	1.2
H186D	26924 ± 2047	34055 ± 1657	0.0067	60 ± 4.1	78.2 ± 5.2	18.2	1.3
H186L	31615 ± 1833	42145 ± 2540	0.0009	70.4 ± 3.4	97.5 ± 8.2	27.1	1.3
H186N	28175 ± 1462	39509 ± 1885	0.0001	63.5 ± 3.1	90.3 ± 5.8	26.8	1.4
H186Q	28845 ± 2365	38865 ± 2966	0.0120	76.9 ± 4.3	105.3 ± 7	28.5	1.4
H186Y	37644 ± 2421	53613 ± 2581	0.0001	83.8 ± 4.5	123.6 ± 8.9	39.8	1.4
M187L	1924 ± 64	12810 ± 929	0.0001	5.3 ± 0.2	34.5 ± 1.9	29.2	6.7
S188A	22589 ± 1833	32197 ± 2515	0.0072	60.6 ± 4	86.3 ± 4.9	25.7	1.4
S188C	18465 ± 1552	25569 ± 2083	0.0033	50.1 ± 3.7	68.6 ± 4.3	18.5	1.4
S188F	7746 ± 839	21273 ± 1477	0.0001	20.7 ± 2	57.1 ± 2.8	36.4	2.8
S188P	BLD	1159 ± 61	0.0001	N/A	3.2 ± 0.2	3.2	NC
S188T	17041 ± 1389	26198 ± 2461	0.0004	45.4 ± 2.5	69.5 ± 4.5	24.0	1.5
S188Y	12244 ± 1167	23849 ± 1725	0.0001	32.6 ± 2.6	64.1 ± 3.5	31.5	2.0
L189S	23204 ± 1213	29510 ± 1181	0.0007	72.6 ± 3.1	92.7 ± 3.2	20.1	1.3
L189V	25544 ± 1758	32031 ± 1633	0.0049	79.9 ± 5.1	100.1 ± 3.9	20.2	1.3
A190D	7141 ± 423	15887 ± 1308	0.0001	22.1 ± 1	49 ± 3.4	26.9	2.2
A190G	24299 ± 2173	34126 ±	0.0030	70.5 ± 7.3	97.9 ± 9.8	27.4	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2992					
A190S	27316 ± 1369	35787 ± 2235	0.0026	84.5 ± 3.2	110.6 ± 5.5	26.1	1.3
A190T	8600 ± 733	18373 ± 795	0.0001	26.3 ± 2	57 ± 1.9	30.7	2.1
A190V	12542 ± 1642	27078 ± 2910	0.0001	36.8 ± 5.1	77.9 ± 9.5	41.2	2.2
L191M	19968 ± 2010	34977 ± 3072	0.0001	58.4 ± 6.6	100.2 ± 9.8	41.7	1.8
L191V	24068 ± 1533	37342 ± 2569	0.0001	71.1 ± 4.7	110.2 ± 7.9	39.1	1.6
N192D	9035 ± 886	28923 ± 1892	0.0001	25.9 ± 3	81.5 ± 6.7	55.6	3.2
N192H	3103 ± 402	8765 ± 935	0.0001	8.6 ± 1.1	24.9 ± 3	16.4	2.8
N192K	8005 ± 776	22845 ± 1943	0.0001	26.3 ± 1.7	76.8 ± 5.6	50.5	2.9
N192S	2470 ± 217	4712 ± 843	0.0003	8.3 ± 0.6	15 ± 1.9	6.6	1.9
N192T	3756 ± 319	8326 ± 1268	0.0001	10.1 ± 0.7	23.5 ± 4	13.4	2.2
R193G	20819 ± 1615	32498 ± 2580	0.0009	64.7 ± 4.1	102.7 ± 7.8	38.0	1.6
R193M	27533 ± 2087	34818 ± 2049	0.0077	68.2 ± 2.7	89.4 ± 5.4	21.2	1.3
R193T	27863 ± 1953	38519 ± 2880	0.0053	70.7 ± 3.6	99.1 ± 7.6	28.4	1.4
R193W	10407 ± 919	21063 ± 1562	0.0001	32 ± 2.4	66.6 ± 4.6	34.6	2.0
T194N	753 ± 80	5923 ± 816	0.0001	2.2 ± 0.2	17.3 ± 2.2	15.1	7.9
T194P	951 ± 71	8134 ± 602	0.0001	2.6 ± 0.3	21.2 ± 1.6	18.6	8.6
T194S	27831 ± 2308	44208 ± 2889	0.0001	69.5 ± 3.9	112.1 ± 6.2	42.6	1.6
G195C	8165 ± 500	13240 ± 568	0.0001	24.6 ± 2.4	39.6 ± 3	15.0	1.6
G195R	15572 ± 893	30415 ± 1008	0.0001	46 ± 3.5	89.4 ± 4.8	43.4	2.0
G195S	20112 ± 883	25947 ± 1235	0.0001	60.5 ± 5	78 ± 6.6	17.5	1.3
R196I	12764 ± 1241	25303 ± 3386	0.0003	30.6 ± 1.8	59.6 ± 5	29.0	2.0
R196K	27718 ± 2086	38090 ± 2117	0.0009	69.8 ± 2.9	97.6 ± 3.2	27.8	1.4
S197C	4181 ± 151	7035 ± 598	0.0002	11.7 ± 0.8	18.3 ± 1	6.5	1.7
S197G	27255 ± 1639	33018 ± 1986	0.0249	72.3 ± 2.1	88.4 ± 3.7	16.1	1.2
S197I	9277 ± 581	18272 ±	0.0001	25.2 ± 1.3	49.5 ± 2.1	24.3	2.0

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1006					
S197N	23664 ± 1103	30051 ± 1440	0.0006	56.9 ± 2.5	72.1 ± 3.3	15.2	1.3
S197T	24022 ± 1698	33425 ± 1713	0.0001	57.6 ± 3.9	79.9 ± 3.6	22.3	1.4
I198M	29416 ± 1526	41174 ± 2420	0.0002	82.3 ± 6.7	113.7 ± 8	31.4	1.4
I198S	1296 ± 63	8455 ± 513	0.0001	3.6 ± 0.3	22.8 ± 1.3	19.2	6.5
V199E	5470 ± 293	15458 ± 855	0.0001	15.2 ± 1.1	41.5 ± 1.9	26.2	2.8
V199L	23090 ± 1117	41654 ± 2281	0.0001	64.4 ± 4.6	113.2 ± 6.6	48.8	1.8
Y200N	3364 ± 193	17117 ± 1368	0.0001	9.5 ± 0.8	46.8 ± 3.5	37.3	5.1
Y200S	514 ± 47	8573 ± 601	0.0001	1.4 ± 0.1	24.4 ± 1.5	22.9	16.7
S201A	37974 ± 2291	47325 ± 1754	0.0024	90.6 ± 5	113.1 ± 3.3	22.5	1.3
S201C	10947 ± 594	23033 ± 1510	0.0001	33.3 ± 2	71.2 ± 6	37.9	2.1
S201T	21522 ± 1510	43648 ± 2695	0.0001	60.5 ± 3.4	122.5 ± 4.4	62.0	2.0
E203A	2061 ± 101	4400 ± 185	0.0001	8.2 ± 0.5	17.3 ± 0.8	9.1	2.1
E203G	12576 ± 575	21197 ± 865	0.0001	48.9 ± 1.9	83.7 ± 4.4	34.8	1.7
E203Q	612 ± 36	2639 ± 161	0.0001	1.9 ± 0.1	8.2 ± 0.7	6.3	4.3
W204S	355 ± 31	7926 ± 612	0.0001	1.4 ± 0.1	30.8 ± 2.2	29.4	22.3
L206F	17666 ± 1621	30374 ± 2385	0.0001	62.9 ± 3.5	111.6 ± 7.6	48.7	1.7
L206H	8805 ± 1133	11278 ± 619	0.0011	26.9 ± 3.5	34.2 ± 1.8	7.4	1.3
L206I	7337 ± 1182	18864 ± 2437	0.0002	25 ± 3.2	66.7 ± 7.2	41.7	2.6
L206R	3629 ± 311	4495 ± 188	0.0104	12.7 ± 1.1	15.8 ± 0.8	3.1	1.2
L206V	16753 ± 1106	30218 ± 1706	0.0001	61.1 ± 2.7	113.7 ± 7.9	52.6	1.8
Y207F	1499 ± 68	3459 ± 412	0.0001	4.8 ± 0.2	10.2 ± 0.9	5.4	2.3
M208K	1899 ± 80	14453 ± 1319	0.0001	6.6 ± 0.3	48.4 ± 3.1	41.9	7.6
W209C	11982 ± 1623	18442 ± 991	0.0001	33.3 ± 4.1	52.8 ± 4.1	19.5	1.5
W209G	27639 ± 2262	35592 ± 1340	0.0005	77.9 ± 6.3	101.9 ± 6.7	24.0	1.3
P210H	20611 ± 1077	32983 ± 1037	0.0001	63.4 ± 2.6	102.9 ± 4	39.5	1.6
P210T	17748 ± 2301	21988 ± 829	0.0077	53.5 ± 6	69.5 ± 3.7	16.0	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
F211C	15289 ± 1161	22737 ± 1182	0.0001	44.4 ± 3.3	65.9 ± 3.1	21.4	1.5
F211L	27936 ± 2981	44713 ± 1823	0.0001	65 ± 5.8	106.5 ± 3.4	41.5	1.6
F211S	22923 ± 1035	34359 ± 1783	0.0001	68 ± 4.4	100.9 ± 5.9	32.9	1.5
F211V	24843 ± 2001	35355 ± 1742	0.0003	72.7 ± 5.9	103.8 ± 5.7	31.1	1.4
F211Y	28160 ± 2206	35233 ± 1670	0.0049	83.4 ± 7.5	104.3 ± 6.5	20.9	1.3
Q212H	32993 ± 2051	40381 ± 2380	0.0049	87.6 ± 4.3	108.6 ± 6	21.0	1.2
Q212P	14401 ± 1189	19918 ± 903	0.0003	37.1 ± 3.5	53.1 ± 3.7	15.9	1.4
K213E	16620 ± 1446	20792 ± 1647	0.0096	37.7 ± 1.9	48.1 ± 2.8	10.4	1.3
K213Q	20448 ± 1811	26374 ± 2372	0.0033	47.1 ± 2.8	60.8 ± 4	13.7	1.3
P214A	18022 ± 1147	36961 ± 1888	0.0001	54.1 ± 4.3	110.2 ± 6.9	56.1	2.1
P214H	1652 ± 116	16179 ± 1128	0.0001	4.8 ± 0.4	46.9 ± 4	42.1	9.8
P214R	25368 ± 1515	46719 ± 2717	0.0001	74.9 ± 4.7	137.3 ± 7.8	62.4	1.8
P214T	14899 ± 1328	36244 ± 2498	0.0001	43.4 ± 4.5	103.9 ± 8.4	60.5	2.4
N215H	7453 ± 631	18621 ± 1170	0.0001	22.2 ± 2.2	55.6 ± 4.2	33.3	2.5
N215K	10660 ± 1166	20220 ± 1700	0.0001	31.6 ± 2.4	61.4 ± 3.3	29.7	1.9
N215T	5392 ± 425	13007 ± 910	0.0001	16.6 ± 1	40 ± 1.7	23.4	2.4
N215Y	2599 ± 259	12737 ± 1218	0.0001	7.4 ± 0.6	36.2 ± 2.8	28.8	4.9
Y216F	30024 ± 2106	37273 ± 1708	0.0026	94.3 ± 6.3	118.9 ± 6.6	24.6	1.2
Y216H	17014 ± 764	27689 ± 1530	0.0001	53.3 ± 1.9	86.7 ± 4.1	33.4	1.6
Y216N	2280 ± 162	19311 ± 1513	0.0001	7 ± 0.6	56.2 ± 3	49.2	8.5
T217A	18943 ± 1372	26939 ± 2043	0.0026	57.8 ± 3.9	81.4 ± 5.2	23.7	1.4
T217I	16049 ± 1284	23470 ± 1933	0.0026	48.1 ± 3.2	70.4 ± 4.8	22.3	1.5
T217K	23428 ± 1823	33844 ±	0.0024	71 ± 4.9	101.9 ± 6.3	30.9	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2556					
T217P	16181 ± 1175	22379 ± 1763	0.0120	49.2 ± 3.4	67.2 ± 4.1	18.0	1.4
T217R	17019 ± 1476	25272 ± 1907	0.0013	51 ± 3.8	75.7 ± 4.5	24.8	1.5
T217S	22763 ± 1515	30767 ± 1213	0.0001	71.8 ± 4.6	98.3 ± 5.3	26.5	1.4
E218A	25638 ± 2941	39175 ± 3493	0.0022	76 ± 7.5	116.7 ± 8.1	40.7	1.5
E218D	33776 ± 2840	43841 ± 3581	0.0072	93.6 ± 8.3	122.7 ± 11.5	29.1	1.3
E218G	7563 ± 677	26769 ± 3204	0.0001	19.9 ± 1.3	68 ± 4.3	48.2	3.5
E218K	12974 ± 1017	27016 ± 2228	0.0001	39.3 ± 2.8	82.1 ± 6	42.8	2.1
E218Q	30758 ± 2592	42487 ± 3621	0.0169	92.7 ± 7	128 ± 9.5	35.3	1.4
E218V	26041 ± 1888	36278 ± 2419	0.0013	71.4 ± 5.3	101.7 ± 8.6	30.3	1.4
I219F	5506 ± 561	29184 ± 2616	0.0001	14.9 ± 1.5	80.6 ± 7.3	65.6	5.3
I219M	8627 ± 769	26166 ± 1736	0.0001	23.6 ± 2.1	71.5 ± 4.3	47.9	3.0
I219S	154 ± 20	3592 ± 274	0.0001	0.4 ± 0.1	10.3 ± 1.1	9.8	23.3
R220L	18399 ± 1213	27014 ± 1455	0.0001	49.7 ± 2.9	73.7 ± 3.6	24.0	1.5
Q221E	30425 ± 2264	37571 ± 2598	0.0360	86.7 ± 6.1	109.5 ± 8.8	22.8	1.2
Q221H	31494 ± 2714	40085 ± 3310	0.0111	87.8 ± 6.6	113.5 ± 8.3	25.7	1.3
Q221K	33217 ± 2944	42352 ± 3561	0.0319	93.5 ± 7.4	122.5 ± 10.4	29.0	1.3
Q221L	31279 ± 2821	39379 ± 3245	0.0158	87.6 ± 7	112.4 ± 8.8	24.9	1.3
Q221R	29462 ± 2455	38738 ± 3284	0.0283	82.1 ± 5.8	110.5 ± 8.7	28.4	1.3
Y222C	21231 ± 1470	32597 ± 1888	0.0001	52.6 ± 2.9	83.5 ± 6.1	30.9	1.5
Y222D	1393 ± 93	12177 ± 1005	0.0001	3.9 ± 0.2	34.5 ± 2.5	30.6	8.7
Y222H	31229 ± 1985	41680 ± 2577	0.0020	87.2 ± 4.4	118.6 ± 6.8	31.4	1.3
Y222N	25948 ± 1953	37634 ±	0.0007	72.1 ± 4.4	107.8 ± 7.2	35.6	1.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2615					
Y222S	22757 ± 1745	35534 ± 2237	0.0001	63.4 ± 4.1	101.2 ± 6.1	37.9	1.6
N224H	26013 ± 2235	42176 ± 3315	0.0006	64.6 ± 5.1	109.2 ± 10.4	44.6	1.6
R227G	1392 ± 71	5084 ± 651	0.0001	3.4 ± 0.1	11.9 ± 1.3	8.5	3.7
N228H	23110 ± 1663	37026 ± 2206	0.0001	56.1 ± 3.7	90.8 ± 5.2	34.7	1.6
N228I	42680 ± 3934	65879 ± 4049	0.0002	102 ± 7.8	158.6 ± 6.1	56.6	1.5
N228T	47321 ± 3640	57308 ± 3851	0.0405	122.7 ± 8.2	149.8 ± 8.1	27.1	1.2
F229I	26139 ± 2203	31786 ± 1919	0.0301	63.2 ± 4.6	77.3 ± 3.6	14.1	1.2
F229S	55992 ± 4881	67601 ± 4129	0.0360	134 ± 9.1	163.4 ± 7.6	29.4	1.2
F229Y	45676 ± 3431	56301 ± 4108	0.0319	110.8 ± 6.6	135.1 ± 7.9	24.3	1.2
A230D	19022 ± 1950	25008 ± 2188	0.0283	62.5 ± 4.5	84 ± 4.8	21.5	1.3
A230G	34550 ± 3372	51722 ± 3294	0.0008	123.1 ± 9.6	189 ± 9.5	65.9	1.5
A230P	18686 ± 1606	27571 ± 2579	0.0072	63.2 ± 4.9	92.7 ± 7.3	29.5	1.5
A230V	30702 ± 2050	40168 ± 2422	0.0039	81.3 ± 4.2	106.6 ± 3.6	25.3	1.3
I232L	1031 ± 81	7224 ± 945	0.0001	2.7 ± 0.2	17.5 ± 1.6	14.9	7.0
I232M	15493 ± 1384	41190 ± 2297	0.0001	38.6 ± 2.2	109.4 ± 8.9	70.8	2.7
I232V	44901 ± 3412	63373 ± 3592	0.0003	113.8 ± 5.7	162.7 ± 7.7	48.9	1.4
D233A	23075 ± 1494	33219 ± 2019	0.0002	59.1 ± 3.1	86.1 ± 5.7	27.0	1.4
D233E	17676 ± 758	23493 ± 924	0.0001	51 ± 2.4	67.3 ± 2.5	16.4	1.3
D233G	15091 ± 776	21651 ± 773	0.0001	41.5 ± 1.9	60 ± 2.4	18.6	1.4
D233V	14655 ± 833	22394 ± 944	0.0001	42.1 ± 2.3	64.1 ± 2.5	22.0	1.5
S235A	1594 ± 58	10500 ± 653	0.0001	4.4 ± 0.1	28.1 ± 1.1	23.7	6.6
S235T	630 ± 54	4696 ± 235	0.0001	1.8 ± 0.1	13.4 ± 0.7	11.6	7.5
K237I	27059 ± 1342	40071 ± 1794	0.0001	79.4 ± 2.6	119 ± 5	39.6	1.5
S238C	4369 ± 302	13891 ± 677	0.0001	12.6 ± 0.9	39 ± 1.3	26.4	3.2
S238I	1456 ± 58	11704 ± 556	0.0001	4.3 ± 0.3	33.8 ± 1.9	29.5	8.0

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
S238T	22557 ± 1256	32589 ± 1426	0.0001	64.7 ± 4	93.7 ± 4.6	29.0	1.4
I239L	15008 ± 905	26331 ± 1039	0.0001	42.7 ± 2.5	75.4 ± 3.3	32.7	1.8
K240E	34180 ± 2424	41878 ± 3056	0.0455	105.2 ± 5.1	130.6 ± 7.9	25.4	1.2
K240M	20450 ± 2148	32367 ± 2715	0.0010	62.4 ± 5.2	99.6 ± 6.2	37.2	1.6
K240R	15131 ± 1420	22482 ± 1791	0.0030	46.8 ± 3.7	70.8 ± 5.5	23.9	1.5
S241C	19490 ± 1584	24585 ± 1839	0.0283	60.5 ± 4.1	75.9 ± 4	15.5	1.3
S241I	18643 ± 1223	39204 ± 2588	0.0001	53.8 ± 2.4	113.8 ± 5.7	60.0	2.1
S241T	29172 ± 2586	38406 ± 3223	0.0057	82.6 ± 4.4	108.9 ± 5.2	26.2	1.3
I242L	20179 ± 1224	33317 ± 2686	0.0001	58.5 ± 2.7	96.2 ± 5.7	37.7	1.7
I242M	2184 ± 180	4826 ± 337	0.0001	6.4 ± 0.5	13.9 ± 0.9	7.5	2.2
I242S	1533 ± 62	15351 ± 937	0.0001	4.8 ± 0.5	44.9 ± 2.5	40.1	10.0
L243M	24772 ± 1493	36055 ± 2526	0.0004	72.7 ± 3.7	104.7 ± 5.3	31.9	1.5
L243S	7839 ± 489	21312 ± 1381	0.0001	23.6 ± 1.8	61.7 ± 2.9	38.1	2.7
L243V	23758 ± 1553	32500 ± 2227	0.0020	68.4 ± 2.7	94.1 ± 4.9	25.7	1.4
D244A	10530 ± 850	20925 ± 1168	0.0001	28.3 ± 1.6	57.5 ± 2.6	29.2	2.0
D244E	16889 ± 1765	31657 ± 1775	0.0001	45.1 ± 3.7	86.8 ± 3.7	41.7	1.9
D244G	9983 ± 848	23926 ± 1422	0.0001	26.8 ± 1.6	64.6 ± 2.2	37.8	2.4
D244V	983 ± 99	7446 ± 537	0.0001	2.8 ± 0.3	20.2 ± 1	17.4	7.6
D244Y	5983 ± 586	15554 ± 1191	0.0001	15.7 ± 1.2	42 ± 2.3	26.3	2.6
W245C	23353 ± 1993	33826 ± 2561	0.0015	63.8 ± 4.2	93.4 ± 6.6	29.7	1.5
T246A	20184 ± 1516	26581 ± 909	0.0001	67.4 ± 5.2	89.3 ± 5.1	21.9	1.3
T246I	18702 ± 1095	29303 ± 1319	0.0001	61.2 ± 3.1	98.8 ± 6.8	37.6	1.6
T246K	BLD	4118 ± 265	0.0001	N/A	14 ± 1.2	14.0	NC
T246R	BLD	1009 ± 64	0.0001	N/A	3.5 ± 0.4	3.5	NC
S247A	24276 ± 1509	29111 ±	0.0045	80 ± 4.9	97.9 ± 7.1	18.0	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1498					
S247F	7957 ± 848	18686 ± 1093	0.0001	25.3 ± 2.1	62.6 ± 4.7	37.3	2.4
S247T	16039 ± 1152	22511 ± 1461	0.0003	53.2 ± 3.9	74.8 ± 5.2	21.6	1.4
S247Y	7433 ± 798	18101 ± 1419	0.0001	23.5 ± 2	60.3 ± 4.9	36.8	2.4
F248C	20087 ± 2973	27351 ± 4250	0.0283	57.9 ± 3.3	77.1 ± 5	19.2	1.4
F248L	21360 ± 3675	28268 ± 4495	0.0072	59.8 ± 4.4	79.5 ± 5.2	19.8	1.3
F248V	20424 ± 2940	27075 ± 4121	0.0429	58.6 ± 3.1	76.7 ± 5	18.1	1.3
F248Y	25850 ± 2314	31204 ± 1758	0.0018	86.6 ± 4.9	107.8 ± 6.1	21.2	1.2
N249D	9050 ± 1262	19080 ± 2665	0.0001	26.6 ± 1.7	55.7 ± 2.8	29.0	2.1
N249H	25157 ± 2681	32119 ± 3556	0.0028	76.1 ± 2.2	96.2 ± 2.9	20.1	1.3
N249I	1864 ± 80	3353 ± 340	0.0014	7.1 ± 0.4	13.1 ± 1.8	6.0	1.8
N249S	7395 ± 926	12077 ± 977	0.0018	26.2 ± 2.9	45.1 ± 4.6	18.9	1.6
N249T	13923 ± 1557	21314 ± 2561	0.0022	42.4 ± 2.8	64.4 ± 3.7	21.9	1.5
N249Y	16445 ± 2008	22166 ± 2504	0.0018	49.4 ± 3.1	66.8 ± 2.5	17.3	1.4
Q250E	8159 ± 688	14252 ± 1068	0.0001	30.2 ± 1.6	52.9 ± 2.4	22.8	1.8
Q250L	2088 ± 234	7820 ± 877	0.0001	7.6 ± 0.6	28.9 ± 3	21.4	3.8
E251G	11980 ± 1124	16458 ± 1113	0.0064	46.1 ± 3.6	64.1 ± 3.3	18.0	1.4
E251K	16089 ± 1970	21714 ± 2048	0.0339	58.7 ± 6	80.8 ± 6.4	22.0	1.4
E251Q	11708 ± 1222	16261 ± 1537	0.0147	43.2 ± 3.6	60.8 ± 4.9	17.6	1.4
E251V	18585 ± 562	24051 ± 593	0.0001	61.6 ± 2.2	81.1 ± 3.9	19.5	1.3
R252G	18020 ± 692	23372 ± 803	0.0001	60.5 ± 3.5	77.9 ± 3.4	17.4	1.3
I253F	21127 ± 1055	26426 ± 1084	0.0018	71.2 ± 3	89 ± 2.7	17.8	1.3
I253N	1319 ± 62	8202 ± 357	0.0001	4.9 ± 0.2	30.6 ± 1.3	25.7	6.2
I253V	28837 ± 2142	37575 ± 3353	0.0053	83.9 ± 5.7	105.4 ± 4.3	21.5	1.3
V254A	23186 ± 1352	30783 ± 1376	0.0006	86.2 ± 4.9	114.5 ± 5	28.3	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
V254D	9616 ± 701	17536 ± 1256	0.0001	36.2 ± 2.9	65.7 ± 4.9	29.5	1.8
V254F	17887 ± 792	25725 ± 1079	0.0001	67 ± 3.5	96.5 ± 4.9	29.5	1.4
V254G	16438 ± 761	23014 ± 1190	0.0001	63.8 ± 3.3	88.3 ± 4	24.5	1.4
D255A	25626 ± 616	30916 ± 1369	0.0020	83.5 ± 2.1	100.1 ± 3.7	16.6	1.2
D255E	23441 ± 971	28215 ± 1532	0.0077	75.6 ± 2.1	90 ± 3	14.4	1.2
D255H	28982 ± 1416	35899 ± 1244	0.0005	93.8 ± 3.8	117 ± 4.2	23.1	1.2
D255N	17034 ± 769	22522 ± 1285	0.0011	66.2 ± 3.3	86.9 ± 4.8	20.7	1.3
D255V	12495 ± 504	17974 ± 1031	0.0002	40.2 ± 0.9	57.4 ± 2.2	17.2	1.4
D255Y	20319 ± 836	25724 ± 1133	0.0004	65.8 ± 2	83.2 ± 2.9	17.5	1.3
V256D	22272 ± 1410	31742 ± 1047	0.0001	77.2 ± 4.4	110.7 ± 3.2	33.5	1.4
V256G	21683 ± 942	30389 ± 884	0.0001	75.2 ± 2.4	106.6 ± 3.8	31.4	1.4
V256L	24022 ± 935	31507 ± 1624	0.0028	77.3 ± 1.7	100.9 ± 3.2	23.6	1.3
A257S	23677 ± 1041	30608 ± 983	0.0001	82.7 ± 3.4	107.4 ± 4	24.7	1.3
G258E	17926 ± 1400	26780 ± 1366	0.0001	62.6 ± 4.8	93.7 ± 4.9	31.1	1.5
P259A	19721 ± 1213	32585 ± 3063	0.0001	57 ± 2.4	91.7 ± 4.4	34.7	1.7
P259T	10040 ± 780	20286 ± 925	0.0001	34.6 ± 2.3	71.2 ± 3.4	36.6	2.0
G260 W	155 ± 55	1188 ± 98	0.0001	0.4 ± 0.1	3.4 ± 0.2	3.0	7.7
G261A	27318 ± 2249	34233 ± 3145	0.0382	79.5 ± 5.9	96.4 ± 4.5	16.9	1.3
N263H	7205 ± 590	22283 ± 1252	0.0001	25.4 ± 2	78.9 ± 4.7	53.6	3.1
N263T	527 ± 54	4649 ± 207	0.0001	1.8 ± 0.2	17.2 ± 1.5	15.4	8.8
D264H	407 ± 21	4188 ± 439	0.0001	1.5 ± 0.1	15.4 ± 2.2	14.0	10.3
D264N	18857 ± 1196	31010 ± 1310	0.0001	66 ± 4.1	110.4 ± 5.7	44.4	1.6
P265A	35589 ± 1537	47153 ± 2302	0.0001	86.9 ± 7.1	114 ± 8.6	27.1	1.3
P265Q	8975 ± 521	31993 ± 1540	0.0001	21 ± 1.1	76.8 ± 5.2	55.8	3.6

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
M267L	2982 ± 411	9684 ± 760	0.0001	8.4 ± 1.1	26.8 ± 1.3	18.4	3.3
M267V	13852 ± 1513	17656 ± 1363	0.0219	39 ± 3.8	50.2 ± 3.5	11.2	1.3
L268F	BLD	3139 ± 435	0.0001	N/A	8 ± 1.1	8.0	NC
L268I	30462 ± 1925	36529 ± 2102	0.0411	74 ± 4.1	90.1 ± 5.3	16.1	1.2
V269L	429 ± 36	4675 ± 523	0.0001	1 ± 0.1	11.7 ± 1.3	10.6	10.9
I270L	36361 ± 2544	46689 ± 3106	0.0104	87.4 ± 3.4	113.7 ± 5.2	26.2	1.3
I270S	274 ± 39	7634 ± 573	0.0001	0.7 ± 0.1	21.3 ± 1.8	20.6	27.9
I270V	30682 ± 2319	37467 ± 2651	0.0301	73.6 ± 3.5	90.3 ± 3.6	16.8	1.2
N272D	28459 ± 2692	39327 ± 2685	0.0024	68.5 ± 4.5	95.9 ± 4.5	27.4	1.4
F273Y	35815 ± 3175	45321 ± 3511	0.0319	82.3 ± 5.6	105.8 ± 6.6	23.5	1.3
L275I	5669 ± 420	22341 ± 1943	0.0001	13.1 ± 0.6	52.8 ± 3.9	39.6	3.9
W277L	28295 ± 2855	37190 ± 3059	0.0234	62 ± 5.8	86.8 ± 10.3	24.9	1.3
N278I	471 ± 67	7024 ± 774	0.0001	1.1 ± 0.1	16.7 ± 1.7	15.6	14.9
Q280L	454 ± 64	8041 ± 943	0.0001	1 ± 0.1	19.2 ± 2.2	18.1	17.7
Q280R	1165 ± 139	10482 ± 1406	0.0001	2.7 ± 0.2	24.8 ± 3.3	22.2	9.0
V281A	27793 ± 1110	45870 ± 2186	0.0001	58.6 ± 3.1	97.1 ± 5.7	38.4	1.7
V281E	23351 ± 783	37701 ± 1194	0.0001	53.1 ± 1.3	85.8 ± 1.9	32.6	1.6
V281G	8729 ± 380	17662 ± 959	0.0001	18.3 ± 0.9	37.4 ± 2.4	19.2	2.0
V281L	30655 ± 1494	38560 ± 1647	0.0007	64.1 ± 3.3	81 ± 4.2	16.9	1.3
T282S	16612 ± 753	25105 ± 1005	0.0001	37.7 ± 1.3	57 ± 1.5	19.3	1.5
Q283E	366 ± 31	6195 ± 415	0.0001	0.8 ± 0.1	13.4 ± 1.2	12.6	16.9
Q283H	32420 ± 1104	44815 ± 1903	0.0001	74.1 ± 2.4	101.7 ± 3.1	27.6	1.4
Q283L	160 ± 25	7906 ± 977	0.0001	0.4 ± 0.1	21.3 ± 1.9	20.9	49.5
M284I	24698 ± 1943	35578 ± 2125	0.0011	58.6 ± 3.7	85.3 ± 3.7	26.7	1.4
M284L	28797 ± 1915	36282 ± 1676	0.0008	65.4 ± 3.7	83.8 ± 4.1	18.4	1.3
A285G	21580 ± 1326	29210 ±	0.0006	51.9 ± 2.5	70.1 ± 2.4	18.2	1.4

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		1510					
A285T	20186 ± 1322	32504 ± 2023	0.0001	45.5 ± 2.4	73.5 ± 3.7	28.0	1.6
A285V	23407 ± 861	32500 ± 1568	0.0001	55.1 ± 2.1	76.5 ± 3.6	21.4	1.4
L286F	29390 ± 1225	39732 ± 2859	0.0004	64.5 ± 2.8	87.7 ± 7.3	23.2	1.4
L286H	359 ± 52	7960 ± 1511	0.0001	0.8 ± 0.1	16.2 ± 2.5	15.4	22.2
L286V	28713 ± 3734	41335 ± 3422	0.0030	66 ± 5.1	98.9 ± 4.3	32.9	1.4
A288G	22208 ± 1755	30458 ± 2381	0.0057	56.8 ± 6.3	76.7 ± 7.4	19.9	1.4
A288S	45790 ± 3395	55988 ± 2609	0.0206	114.6 ± 10.6	140.4 ± 10.5	25.8	1.2
A288V	32777 ± 3168	45501 ± 4634	0.0193	82.5 ± 9	114.2 ± 12.4	31.7	1.4
I289L	37941 ± 3208	49640 ± 3368	0.0077	96.9 ± 10.5	124.4 ± 11.3	27.5	1.3
I289T	15033 ± 1450	29673 ± 2480	0.0001	38.6 ± 4.8	75.3 ± 7.9	36.7	2.0
I289V	25845 ± 1706	31489 ± 1397	0.0039	61.2 ± 3.2	74.8 ± 2.7	13.6	1.2
A291G	6953 ± 474	16073 ± 954	0.0001	26.6 ± 1.5	61.5 ± 2.6	34.9	2.3
A292G	12091 ± 652	19406 ± 1361	0.0001	41.1 ± 2.2	65.3 ± 4	24.3	1.6
A292S	18002 ± 1127	23779 ± 1584	0.0077	68.6 ± 2.9	89.9 ± 3.4	21.3	1.3
L294F	10147 ± 971	23486 ± 2100	0.0001	29.6 ± 3	68.4 ± 6.5	38.8	2.3
L294I	8345 ± 717	26761 ± 1915	0.0001	24.8 ± 2.4	78.4 ± 6	53.6	3.2
L294V	1452 ± 71	13038 ± 880	0.0001	4.4 ± 0.3	38.2 ± 2.7	33.8	9.0
F295I	26687 ± 1470	35634 ± 2203	0.0013	78.3 ± 4.5	104.1 ± 6.6	25.7	1.3
F295S	230 ± 45	3847 ± 309	0.0001	0.6 ± 0.1	11.1 ± 0.9	10.5	16.8
F295V	24973 ± 1752	41782 ± 2877	0.0001	73.4 ± 5.7	121.5 ± 7.7	48.0	1.7
F295Y	21452 ± 1929	34502 ± 2504	0.0003	62.9 ± 6.1	99.2 ± 6.5	36.3	1.6
S297T	BLD	3178 ± 327	0.0001	N/A	9.7 ± 0.8	9.7	NC
N298D	795 ± 56	7645 ± 388	0.0001	2.5 ± 0.2	24.2 ± 1.2	21.7	9.6
N298I	2942 ± 262	13906 ± 535	0.0001	9.2 ± 0.7	44.1 ± 1.8	34.9	4.7

Table 7

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N298T	20581 ± 1736	25249 ± 1705	0.0033	61.2 ± 4.7	75.4 ± 4.3	14.2	1.2
D299H	358 ± 36	8424 ± 875	0.0001	1 ± 0.1	23.1 ± 2.4	22.1	23.5
D299N	11973 ± 1961	14668 ± 809	0.0005	29.2 ± 4.7	37.1 ± 2.9	7.8	1.2
L300I	7328 ± 448	19317 ± 757	0.0001	20.7 ± 0.9	55.1 ± 2	34.4	2.6
L300V	406 ± 48	5354 ± 203	0.0001	1.3 ± 0.2	15.3 ± 0.6	14.0	13.2
H302D	32677 ± 1437	41716 ± 1847	0.0008	95.1 ± 5.8	120.8 ± 6.6	25.8	1.3
H302L	24188 ± 1797	34251 ± 1760	0.0001	60.7 ± 5.1	85.3 ± 4.7	24.6	1.4
H302N	31958 ± 1777	42296 ± 2028	0.0003	91.2 ± 4.3	121.4 ± 6.2	30.2	1.3
H302Y	22554 ± 1372	31688 ± 1241	0.0001	59 ± 3.5	84.2 ± 5.2	25.3	1.4
I303S	BLD	1496 ± 117	0.0001	N/A	3.8 ± 0.3	3.8	NC
S304I	11675 ± 939	17257 ± 1837	0.0072	30.6 ± 1.4	44.6 ± 2.4	13.9	1.5
Q306E	31745 ± 2212	39019 ± 2405	0.0169	82 ± 2.8	101.7 ± 4.2	19.7	1.2
Q306L	19792 ± 1899	26515 ± 1960	0.0147	56.9 ± 4	76.4 ± 3.4	19.6	1.3
Q306P	19933 ± 1648	29495 ± 1671	0.0004	57.4 ± 2.8	87.5 ± 4.8	30.0	1.5
A307D	42522 ± 2430	54502 ± 3031	0.0026	126 ± 5.7	161.9 ± 8.6	35.9	1.3
A307G	17871 ± 1029	26053 ± 1631	0.0006	52.9 ± 2.5	76.3 ± 3.1	23.4	1.5
A307P	11388 ± 905	15572 ± 1124	0.0072	32.8 ± 1.7	45.2 ± 2.1	12.3	1.4
A307S	29300 ± 2037	38558 ± 2274	0.0026	85.9 ± 4.5	113.6 ± 5.2	27.7	1.3
A307V	11478 ± 1200	25989 ± 2015	0.0001	27.5 ± 2	62.2 ± 3.3	34.7	2.3
K308I	19195 ± 1555	29251 ± 2026	0.0005	48.6 ± 3.9	72.7 ± 3.6	24.2	1.5
K308Q	24208 ± 1996	35663 ± 2680	0.0022	59.1 ± 3.8	89.1 ± 5.5	30.0	1.5
K308R	27103 ± 1767	35824 ± 2438	0.0057	68.9 ± 4.3	89.1 ± 4.5	20.3	1.3
A309D	31696 ± 3036	38325 ± 2376	0.0077	78.3 ± 5.2	95.8 ± 3.7	17.6	1.2
A309T	29214 ± 1907	36228 ± 1841	0.0067	74.1 ± 4.6	92.7 ± 4.8	18.6	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
L310I	31871 ± 2599	40310 ± 3345	0.0266	72.8 ± 3.6	92.4 ± 5.1	19.6	1.3
L311I	4020 ± 235	11558 ± 781	0.0001	12.1 ± 0.8	35.3 ± 3.1	23.2	2.9
Q312E	1365 ± 57	6331 ± 466	0.0001	4.1 ± 0.2	19.2 ± 1.7	15.1	4.6
Q312K	6733 ± 510	11934 ± 624	0.0001	19.7 ± 1.4	35.2 ± 1.8	15.5	1.8
Q312L	16986 ± 1428	23967 ± 1400	0.0011	50.1 ± 4.1	71.5 ± 4.6	21.3	1.4
D313E	14321 ± 1579	18273 ± 1330	0.0014	42.5 ± 2.3	55.7 ± 1.9	13.2	1.3
D313V	894 ± 33	3480 ± 580	0.0001	2.9 ± 0.2	9.6 ± 0.9	6.7	3.9
K314E	13026 ± 1767	16765 ± 2098	0.0033	37.7 ± 2.5	48.7 ± 2.8	11.0	1.3
K314M	18231 ± 2878	23043 ± 2838	0.0014	50.9 ± 3.8	66.8 ± 3.8	15.9	1.3
K314N	14205 ± 2418	17364 ± 2225	0.0022	39.1 ± 3.4	49.9 ± 2.6	10.8	1.2
K314T	25162 ± 2701	30501 ± 2332	0.0036	75.9 ± 4.4	93.8 ± 4.5	17.9	1.2
D315A	18519 ± 1370	24758 ± 1512	0.0036	68.3 ± 4.8	93.4 ± 7	25.1	1.3
D315G	13326 ± 859	19115 ± 1697	0.0042	49.7 ± 3.7	73.3 ± 8	23.6	1.4
D315H	9791 ± 1077	14136 ± 1573	0.0030	35.7 ± 2.8	53.2 ± 5.5	17.4	1.4
D315N	8553 ± 425	13037 ± 869	0.0001	34.1 ± 1.7	52.1 ± 3.7	17.9	1.5
D315V	8191 ± 717	14580 ± 1235	0.0001	31.2 ± 3.6	56 ± 6	24.8	1.8
D315Y	9198 ± 1179	12674 ± 1008	0.0206	34.5 ± 3.5	48.7 ± 2.4	14.2	1.4
V316A	13166 ± 1029	18908 ± 1577	0.0033	48.8 ± 4.1	71.5 ± 7.1	22.7	1.4
V316L	12854 ± 958	21812 ± 1450	0.0001	47.4 ± 3.9	81.3 ± 6.3	33.9	1.7
I317L	14780 ± 1222	18770 ± 1141	0.0199	54.4 ± 4.9	70.9 ± 5.6	16.5	1.3
I317M	340 ± 29	3988 ± 177	0.0001	1 ± 0.1	11.2 ± 0.8	10.2	11.7
I317V	14885 ± 1495	19927 ± 1565	0.0147	55 ± 6.1	73.6 ± 5.5	18.6	1.3
A318D	15357 ± 1499	20838 ± 1817	0.0012	42.5 ± 3.6	59.4 ± 5.3	16.9	1.4
A318P	526 ± 42	2799 ± 174	0.0001	1.5 ± 0.2	8 ± 0.8	6.5	5.3
A318T	16954 ± 1483	22296 ± 1232	0.0009	45.2 ± 2.8	62.9 ± 4.6	17.7	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
A318V	14603 ± 1377	19658 ± 1108	0.0022	37.9 ± 2.1	54.4 ± 3.5	16.5	1.4
I319M	12191 ± 433	14802 ± 727	0.0047	47.4 ± 2.2	56.8 ± 2.3	9.4	1.2
N320S	21562 ± 1285	28097 ± 1522	0.0022	82.9 ± 4.5	106.7 ± 3.9	23.9	1.3
N320T	5597 ± 442	11276 ± 658	0.0001	21.6 ± 1.5	43.3 ± 1.9	21.8	2.0
Q321K	7590 ± 520	16046 ± 870	0.0001	29.2 ± 2	61.2 ± 2.4	32.0	2.1
D322A	1908 ± 139	6170 ± 310	0.0001	6.8 ± 0.4	22.2 ± 1	15.3	3.2
D322V	714 ± 53	3989 ± 217	0.0001	2.6 ± 0.2	14.3 ± 0.6	11.7	5.6
L324V	17027 ± 1167	20866 ± 1331	0.0090	57.2 ± 2.1	70.2 ± 2	13.0	1.2
L324W	20623 ± 721	25772 ± 1045	0.0004	73.5 ± 1.8	93.3 ± 4.5	19.8	1.3
G325A	18183 ± 1254	27523 ± 1456	0.0001	64.9 ± 3.8	99.2 ± 5.4	34.4	1.5
G325C	14482 ± 695	23873 ± 1021	0.0001	51.4 ± 1.7	85.9 ± 4	34.5	1.7
G325V	572 ± 30	5333 ± 294	0.0001	2.2 ± 0.2	19.3 ± 1.1	17.1	9.3
K326E	15541 ± 832	22340 ± 828	0.0001	55.6 ± 2.6	80.9 ± 3.9	25.3	1.4
K326M	8482 ± 500	31204 ± 1979	0.0001	24.4 ± 1.6	87.6 ± 3.5	63.2	3.7
K326Q	22075 ± 1209	29168 ± 1869	0.0010	78 ± 3	104.1 ± 5.7	26.1	1.3
K326R	17744 ± 923	31690 ± 1112	0.0001	61.7 ± 3.4	109.7 ± 2.9	48.0	1.8
K326T	19442 ± 739	26653 ± 877	0.0001	69.6 ± 2.4	96 ± 3.7	26.4	1.4
Q327H	BLD	2197 ± 226	0.0001	N/A	7.4 ± 0.7	7.4	NC
Q327P	7775 ± 561	18612 ± 1075	0.0001	26.2 ± 1.8	62.6 ± 3.1	36.4	2.4
Y329C	9148 ± 414	11442 ± 480	0.0011	31.2 ± 1.5	38.9 ± 1.6	7.8	1.3
Y329D	1249 ± 66	4917 ± 181	0.0001	4.2 ± 0.2	16.7 ± 0.6	12.5	3.9
Y329F	10368 ± 646	15566 ± 603	0.0001	30.6 ± 1.5	47.1 ± 2.8	16.6	1.5
Y329H	13757 ± 963	18672 ± 772	0.0002	47.2 ± 3.8	63.4 ± 2.6	16.2	1.4
Y329N	6448 ± 436	11035 ± 429	0.0001	21.8 ± 1.5	37.4 ± 1.2	15.6	1.7
Q330E	7500 ± 345	13086 ± 589	0.0001	26.4 ± 1.5	46.4 ± 2.6	19.9	1.7
Q330H	9296 ± 649	20752 ± 592	0.0001	33.1 ± 2.8	73.9 ± 3.6	40.8	2.2
Q330K	20289 ± 720	26149 ± 1074	0.0001	71 ± 2.7	92.1 ± 4.2	21.1	1.3
L331H	11743 ± 634	19003 ± 791	0.0001	42 ± 3.2	67.9 ± 4.3	25.9	1.6
L331P	157 ± 20	1029 ± 32	0.0001	0.6 ± 0.1	3.7 ± 0.2	3.1	6.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
L331R	9725 ± 634	15841 ± 639	0.0001	33.2 ± 1.5	56.5 ± 3.2	23.3	1.6
L331V	25163 ± 801	33050 ± 967	0.0001	89.4 ± 4.5	117.4 ± 5.6	28.0	1.3
R332G	33043 ± 1431	42737 ± 1959	0.0002	78.8 ± 2.7	102.3 ± 4.6	23.4	1.3
R332I	24614 ± 1678	41550 ± 2461	0.0001	63.3 ± 4.5	106.6 ± 6.4	43.2	1.7
R332S	33936 ± 2528	41700 ± 2778	0.0193	87.6 ± 6.6	108.1 ± 8.4	20.5	1.2
R332T	26141 ± 1254	39363 ± 2176	0.0001	73.3 ± 2.9	109.5 ± 4.7	36.2	1.5
Q333E	30291 ± 2094	38709 ± 2428	0.0067	77.8 ± 5.3	101.3 ± 7.6	23.5	1.3
Q333L	25450 ± 2094	33727 ± 1965	0.0042	68.6 ± 2.9	93.3 ± 4.1	24.7	1.3
Q333P	11819 ± 1039	22746 ± 1255	0.0001	30.3 ± 1.7	61.3 ± 3.9	31.0	1.9
G334R	25886 ± 3237	31174 ± 2016	0.0429	58.9 ± 4.6	76.4 ± 2.7	17.5	1.2
G334V	31991 ± 2390	38301 ± 2744	0.0219	68.4 ± 3.2	82.1 ± 3.8	13.7	1.2
D335A	21055 ± 1662	33829 ± 4641	0.0120	57.9 ± 3	85.6 ± 6.9	27.7	1.6
D335E	30532 ± 1962	39124 ± 2722	0.0053	68.7 ± 4.8	86.5 ± 4.5	17.7	1.3
D335G	22766 ± 1355	30341 ± 3325	0.0234	51.3 ± 2.8	67 ± 5.6	15.7	1.3
D335V	7938 ± 336	16557 ± 929	0.0001	18.1 ± 0.6	37.5 ± 1.6	19.4	2.1
D335Y	19469 ± 982	24732 ± 2214	0.0147	43 ± 1.7	54.1 ± 3.5	11.0	1.3
N336D	23869 ± 1072	39534 ± 2519	0.0001	53.7 ± 2.8	88.1 ± 4.9	34.3	1.7
N336I	8544 ± 1083	18303 ± 1404	0.0001	20.7 ± 2.7	43.8 ± 1.6	23.0	2.1
N336S	32974 ± 2396	40651 ± 2487	0.0169	79.7 ± 3.8	98.4 ± 3.1	18.7	1.2
N336T	12743 ± 709	25898 ± 1374	0.0001	28.9 ± 1.3	58.6 ± 2.3	29.7	2.0
N336Y	29615 ± 1640	37475 ± 2540	0.0045	66.3 ± 3.7	83 ± 4.4	16.6	1.3
F337C	9557 ± 452	17991 ± 960	0.0001	21.7 ± 0.8	40.7 ± 1.6	19.0	1.9
F337L	23197 ± 2254	31963 ± 2641	0.0022	57.8 ± 4.8	78.6 ± 3.1	20.8	1.4
F337V	29582 ± 2747	42718 ±	0.0007	65.9 ± 4.1	97 ± 4.6	31.1	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2776					
F337Y	21577 ± 1930	30991 ± 2695	0.0023	52.3 ± 4.2	73.9 ± 3.2	21.6	1.4
E338A	15626 ± 769	25719 ± 1376	0.0001	39.5 ± 2.3	64.3 ± 3	24.8	1.7
E338D	25700 ± 1958	31632 ± 1825	0.0033	65.7 ± 4.9	80.9 ± 4.6	15.2	1.2
E338G	6415 ± 391	12588 ± 538	0.0001	17.1 ± 1.1	33.9 ± 1.8	16.8	2.0
V339M	26113 ± 1116	33867 ± 2526	0.0030	63.5 ± 2.9	81.7 ± 5	18.2	1.3
E341A	1444 ± 159	5855 ± 690	0.0001	3.8 ± 0.4	15.4 ± 1.3	11.6	4.1
E341Q	20802 ± 2164	28411 ± 2891	0.0294	55.5 ± 3.7	75.2 ± 4.1	19.7	1.4
P343A	25254 ± 2385	32890 ± 2292	0.0062	69.5 ± 4.9	90.7 ± 3.7	21.2	1.3
P343S	22132 ± 1243	29289 ± 2351	0.0147	62.1 ± 2.7	81.1 ± 4.6	19.0	1.3
L344F	217 ± 25	3629 ± 614	0.0001	0.6 ± 0.1	9.6 ± 1.4	9.0	16.7
L344R	4983 ± 848	11592 ± 1593	0.0006	10.9 ± 1.4	26.2 ± 2.6	15.3	2.3
L344V	13586 ± 1026	19262 ± 903	0.0002	40.6 ± 3.2	57.5 ± 2.5	16.8	1.4
G346A	23263 ± 1479	31948 ± 1306	0.0001	58.3 ± 3.3	80.4 ± 2.8	22.0	1.4
G346C	18258 ± 1054	22856 ± 1772	0.0206	39.5 ± 1.9	49.2 ± 2.9	9.7	1.3
G346D	31327 ± 3822	46560 ± 3904	0.0053	67.5 ± 6.4	103.3 ± 6	35.8	1.5
G346V	11683 ± 1406	20902 ± 2356	0.0012	28.8 ± 2.4	51.4 ± 3.9	22.7	1.8
L347I	26815 ± 2533	33517 ± 2802	0.0429	65 ± 3.8	82.4 ± 5	17.4	1.3
A348D	21682 ± 817	26025 ± 1129	0.0030	41.6 ± 1.5	50 ± 2.2	8.4	1.2
W349C	17800 ± 1182	23210 ± 1299	0.0009	41.5 ± 2.6	53.7 ± 2.5	12.3	1.3
W349L	18128 ± 742	24184 ± 1517	0.0013	35 ± 1.6	46.8 ± 3.2	11.8	1.3
A350G	21459 ± 695	26360 ± 1002	0.0012	41 ± 0.9	50.5 ± 1.7	9.5	1.2
A350S	26493 ± 1291	34474 ± 1484	0.0004	62.9 ± 4.2	80.5 ± 3.6	17.6	1.3
A350T	20227 ± 1499	26484 ± 1189	0.0013	47.4 ± 3.7	61.7 ± 2.7	14.4	1.3

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
A350V	12786 ± 654	22855 ± 1012	0.0001	27.9 ± 0.9	50.2 ± 1.6	22.3	1.8
V351A	24009 ± 1662	30218 ± 1531	0.0053	56.9 ± 4.7	71.1 ± 4.1	14.2	1.3
V351E	4760 ± 281	7910 ± 348	0.0001	10.5 ± 0.5	17.7 ± 1	7.2	1.7
A352S	23476 ± 1901	28397 ± 1310	0.0169	52.8 ± 3.7	64.9 ± 2.5	12.1	1.2
A352T	15803 ± 777	29351 ± 1532	0.0001	37.2 ± 2.1	68.2 ± 3.2	31.0	1.9
M353K	13638 ± 804	19335 ± 946	0.0003	30.3 ± 1.8	43.4 ± 2.6	13.0	1.4
M353L	30347 ± 1572	36987 ± 1768	0.0083	66.6 ± 2.7	81.2 ± 2.7	14.6	1.2
M353T	15631 ± 1026	21953 ± 937	0.0001	46.4 ± 2.8	65.6 ± 3	19.2	1.4
I354R	9157 ± 633	21854 ± 1398	0.0001	20.1 ± 1.2	47.9 ± 2.6	27.8	2.4
N355D	3366 ± 241	11004 ± 832	0.0001	7.3 ± 0.4	24 ± 1.6	16.7	3.3
N355H	1822 ± 81	6399 ± 338	0.0001	4 ± 0.2	13.9 ± 0.6	9.9	3.5
N355S	11397 ± 817	24820 ± 1396	0.0001	25.9 ± 1.6	56.7 ± 2.8	30.8	2.2
N355Y	5994 ± 461	16930 ± 1745	0.0001	15.2 ± 1	41.8 ± 3.3	26.6	2.8
R356L	10680 ± 518	29548 ± 2017	0.0001	24.4 ± 1	68.1 ± 4.6	43.7	2.8
Q357E	15264 ± 877	28922 ± 1194	0.0001	42.8 ± 2.1	84.3 ± 6.3	41.5	1.9
I359F	6138 ± 568	13144 ± 1091	0.0001	13 ± 1	27 ± 1.6	14.1	2.1
I359L	16254 ± 909	26791 ± 1713	0.0001	39.1 ± 1.8	64.7 ± 3.9	25.6	1.7
I359N	10862 ± 655	17332 ± 879	0.0001	20.8 ± 1.2	33.3 ± 1.8	12.5	1.6
I359S	37737 ± 2594	48055 ± 2727	0.0067	101.6 ± 6.3	131.2 ± 8.4	29.6	1.3
I359V	20990 ± 1174	34265 ± 1528	0.0001	51.5 ± 3.4	83.1 ± 3.3	31.6	1.6
P362A	35322 ± 3087	49809 ± 2721	0.0007	100.8 ± 9.5	140.9 ± 8.5	40.1	1.4
P362H	3713 ± 377	14620 ± 531	0.0001	11.2 ± 1	44.6 ± 1.9	33.4	3.9
P362R	8745 ± 1176	15971 ± 1019	0.0001	25 ± 3.1	48.9 ± 4.1	23.9	1.8
P362S	25234 ± 2794	45209 ± 4138	0.0003	71.2 ± 7.7	125 ± 9	53.8	1.8
R363G	13990 ± 1613	37837 ±	0.0001	41.8 ± 5.1	114.4 ±	72.6	2.7

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α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2998			10.7		
R363L	8123 ± 869	27997 ± 2485	0.0001	23.2 ± 1.9	85.4 ± 9.5	62.2	3.5
R363S	16400 ± 1695	44621 ± 3266	0.0001	50.1 ± 5.9	136.7 ± 12.4	86.6	2.7
S364C	41263 ± 2389	53912 ± 3067	0.0020	127 ± 10.6	167 ± 14.8	40.0	1.3
S364P	48193 ± 4573	66731 ± 4698	0.0062	143.2 ± 13.7	206.4 ± 20	63.1	1.4
Y365D	9119 ± 1027	14664 ± 1311	0.0013	31.3 ± 2.7	51 ± 3.5	19.7	1.6
Y365F	19631 ± 2010	25395 ± 2160	0.0266	67.7 ± 5.1	88.8 ± 5.3	21.1	1.3
Y365N	19111 ± 869	26514 ± 1978	0.0002	59.7 ± 1.7	82.2 ± 4.5	22.5	1.4
Y365S	14346 ± 1563	19484 ± 1899	0.0180	49.4 ± 4.1	67.8 ± 4.9	18.4	1.4
T366I	18539 ± 1165	24814 ± 1897	0.0045	57.8 ± 2.5	77.8 ± 5.3	20.0	1.3
T366N	24650 ± 1756	30947 ± 1867	0.0137	78.1 ± 5.3	98.5 ± 5.4	20.4	1.3
T366P	13407 ± 1462	16910 ± 1608	0.0455	46.2 ± 4	59.5 ± 5.1	13.4	1.3
T366S	20731 ± 2170	24885 ± 1760	0.0301	70.6 ± 4.9	86.7 ± 3.6	16.2	1.2
I367F	15728 ± 1680	22178 ± 1794	0.0020	48.3 ± 3.7	69.9 ± 5.7	21.6	1.4
I367L	25211 ± 1640	31257 ± 2256	0.0339	79 ± 4	101 ± 9.3	21.9	1.2
I367M	28430 ± 1769	36008 ± 2249	0.0104	76.7 ± 3.9	99 ± 6.7	22.3	1.3
A368G	31616 ± 2552	42198 ± 2923	0.0111	83.9 ± 4.7	114.8 ± 7.8	30.9	1.3
A368P	26402 ± 926	33525 ± 1803	0.0001	91.7 ± 4.6	117.4 ± 8.7	25.7	1.3
V369A	23968 ± 1797	35925 ± 2462	0.0006	77.6 ± 5	116.2 ± 6.3	38.6	1.5
V369F	11912 ± 1197	18282 ± 1960	0.0137	37.7 ± 2.8	57.3 ± 4.8	19.6	1.5
V369G	803 ± 59	2628 ± 291	0.0001	2.6 ± 0.2	8.1 ± 0.7	5.5	3.3
V369I	30094 ± 3211	36630 ± 2373	0.0206	79.7 ± 6.8	99.3 ± 5.5	19.6	1.2
V369L	27680 ± 1912	38458 ±	0.0014	74.2 ± 3.7	104.5 ± 5.6	30.3	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		2367					
A370D	27098 ± 2504	33279 ± 2473	0.0405	87.5 ± 6.1	109.8 ± 6.8	22.4	1.2
A370G	24835 ± 2637	31805 ± 3001	0.0382	78.1 ± 4.4	101 ± 5.4	22.9	1.3
A370P	10431 ± 975	15618 ± 1776	0.0020	33.9 ± 2.8	50.7 ± 5.4	16.9	1.5
A370T	25024 ± 1951	30276 ± 2364	0.0481	79.9 ± 4.3	97.5 ± 6.1	17.6	1.2
A370V	15754 ± 1222	24151 ± 1591	0.0003	40.1 ± 3.1	60.7 ± 3.5	20.6	1.5
S371C	10189 ± 1078	14546 ± 1141	0.0022	23.5 ± 1.3	34.7 ± 1.6	11.1	1.4
S371T	27962 ± 2785	37065 ± 2351	0.0028	65 ± 3.3	91.1 ± 5	26.1	1.3
G373A	14426 ± 630	18622 ± 1289	0.0011	40.8 ± 1.5	53.2 ± 3.7	12.4	1.3
G373C	1744 ± 92	5543 ± 547	0.0001	4.3 ± 0.2	13 ± 0.9	8.7	3.2
K374E	19699 ± 1718	24879 ± 2423	0.0429	49.9 ± 3.6	64 ± 5.7	14.1	1.3
K374I	8194 ± 506	16076 ± 936	0.0001	22.3 ± 1.3	44.2 ± 2.9	21.9	2.0
K374R	27984 ± 2321	34403 ± 2426	0.0147	74.3 ± 4.8	92.2 ± 4.9	17.9	1.2
K374T	16418 ± 1050	26614 ± 1659	0.0001	46.1 ± 2.8	76.2 ± 5.7	30.2	1.6
G375R	15302 ± 1157	22033 ± 1442	0.0015	41.7 ± 1.9	60.4 ± 2.1	18.7	1.4
V376E	22992 ± 924	30929 ± 1635	0.0003	74 ± 4.6	95.9 ± 3.8	21.9	1.4
V376G	33903 ± 2255	44774 ± 2982	0.0036	93.9 ± 4.6	122.9 ± 5.6	28.9	1.3
V376L	27275 ± 1181	34152 ± 1845	0.0062	82.4 ± 3.4	102.3 ± 4.2	19.9	1.3
V376M	27547 ± 1431	34563 ± 1762	0.0024	79.3 ± 2.7	99.4 ± 3.2	20.1	1.3
A377G	26583 ± 1072	32517 ± 981	0.0006	71.6 ± 2.5	87.7 ± 2.3	16.1	1.2
A377P	21842 ± 930	28189 ± 1292	0.0004	59.4 ± 2.6	76.6 ± 3.5	17.2	1.3
A377S	17737 ± 860	22793 ± 999	0.0004	48.1 ± 2.3	61.8 ± 2.7	13.7	1.3
A377T	15839 ± 802	20817 ± 838	0.0003	42.5 ± 1.9	56.1 ± 2	13.5	1.3
N379D	4128 ± 1118	5604 ± 979	0.0339	9.4 ± 2.2	13.1 ± 1.9	3.8	1.4
N379I	13128 ± 1712	17862 ± 1825	0.0057	28.7 ± 2.7	40 ± 2.8	11.4	1.4

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α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
N379K	31962 ± 2268	40568 ± 2417	0.0083	74.6 ± 3.3	95 ± 2.7	20.4	1.3
N379T	18827 ± 1525	23023 ± 1524	0.0266	43.2 ± 2.7	52.9 ± 2.7	9.8	1.2
P380A	9820 ± 705	17454 ± 1133	0.0001	23.2 ± 1.7	40.7 ± 2.3	17.5	1.8
P380H	10463 ± 941	17759 ± 1310	0.0001	23.7 ± 1.4	41.1 ± 2.2	17.4	1.7
P380R	14432 ± 1315	21330 ± 1744	0.0083	37.8 ± 5	52.4 ± 3.4	14.6	1.5
P380T	10544 ± 669	13919 ± 666	0.0013	24.2 ± 1.1	32.2 ± 1	8.0	1.3
A381D	20587 ± 1974	30666 ± 2629	0.0015	46.7 ± 3	71.4 ± 5	24.7	1.5
F383C	22779 ± 2557	29945 ± 3409	0.0339	59.6 ± 4.6	79 ± 6.8	19.3	1.3
F383I	31554 ± 2813	39170 ± 2761	0.0169	81.7 ± 5.6	104.2 ± 8	22.6	1.2
F383Y	28986 ± 2572	39286 ± 2306	0.0057	73.7 ± 3.8	105.1 ± 6	31.4	1.4
I384F	4673 ± 750	7946 ± 807	0.0012	11.1 ± 1.3	19.7 ± 1.6	8.6	1.7
I384M	15481 ± 1665	20745 ± 1623	0.0036	39.7 ± 3	54.5 ± 3.7	14.8	1.3
I384T	4755 ± 673	8160 ± 1059	0.0062	12.3 ± 1.6	20.5 ± 2.4	8.2	1.7
T385I	18236 ± 2074	23597 ± 1843	0.0018	43.4 ± 3.3	56.1 ± 2.4	12.7	1.3
Q386H	1148 ± 70	2424 ± 353	0.0002	4.1 ± 0.3	8.1 ± 0.9	3.9	2.1
Q386K	7135 ± 749	9850 ± 1061	0.0219	17.2 ± 1.6	23.1 ± 1.8	5.9	1.4
Q386L	7326 ± 646	9698 ± 839	0.0219	17.8 ± 1.4	23.1 ± 1.5	5.3	1.3
L387F	17188 ± 1822	21003 ± 1547	0.0234	59.1 ± 4.9	72.6 ± 4.5	13.5	1.2
L387H	16827 ± 1557	23648 ± 1827	0.0030	58.8 ± 4.7	81.3 ± 4.6	22.5	1.4
L387I	28707 ± 3510	36657 ± 3056	0.0062	95.8 ± 6.8	123.7 ± 5.1	28.0	1.3
L387R	11133 ± 1516	15211 ± 1727	0.0249	28.2 ± 3.6	39.4 ± 4.4	11.2	1.4
L388F	12563 ± 1654	17583 ± 1509	0.0030	32.1 ± 4.2	45 ± 3.4	12.9	1.4
L388H	1354 ± 89	7341 ± 518	0.0001	3.2 ± 0.2	17.2 ± 1	13.9	5.4
L388I	18562 ± 2245	24746 ± 2326	0.0249	46.6 ± 5.2	64.2 ± 6	17.6	1.3
L388R	1833 ± 101	5072 ± 627	0.0001	4.4 ± 0.3	12.2 ± 1.5	7.8	2.8

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
L388V	15962 ± 1927	25028 ± 2179	0.0018	39.3 ± 3.6	65 ± 5.6	25.7	1.6
K391I	1544 ± 98	5343 ± 587	0.0001	4.3 ± 0.3	14.1 ± 1.4	9.9	3.5
K391N	23114 ± 1999	30489 ± 2411	0.0111	60.5 ± 5.2	78.3 ± 5.4	17.9	1.3
K391Q	20154 ± 2061	30714 ± 2783	0.0028	51.5 ± 4.6	76.6 ± 4.7	25.2	1.5
K391R	26395 ± 2258	33349 ± 2491	0.0158	69.1 ± 6	85.9 ± 4.8	16.8	1.3
R392G	21151 ± 1706	26480 ± 2033	0.0249	59.1 ± 5.3	72.1 ± 5	13.0	1.3
R392K	33729 ± 2386	42707 ± 2665	0.0057	98.7 ± 6.6	125.9 ± 8.5	27.2	1.3
R392M	32856 ± 2534	41635 ± 1964	0.0042	97.2 ± 6.1	125.2 ± 5.2	27.9	1.3
R392 W	17580 ± 1671	22596 ± 1839	0.0219	46.9 ± 4.8	58.2 ± 4.1	11.4	1.3
K393E	16648 ± 1284	32275 ± 1905	0.0001	50.5 ± 3.8	98.3 ± 6.2	47.9	1.9
K393N	23262 ± 1719	30064 ± 1959	0.0007	68.3 ± 7.8	86.6 ± 8.7	18.3	1.3
K393Q	19722 ± 1445	32686 ± 1866	0.0001	60.3 ± 4.6	99.9 ± 6.6	39.6	1.7
K393T	18084 ± 1183	23886 ± 1214	0.0009	55.7 ± 4.1	73.6 ± 4.8	17.9	1.3
L394I	30400 ± 2425	41644 ± 3334	0.0067	98.5 ± 13	135.5 ± 17.6	37.0	1.4
L394Q	11635 ± 1091	17701 ± 1268	0.0006	36.5 ± 5.1	57 ± 6.8	20.5	1.5
L394R	16836 ± 1562	25594 ± 1826	0.0005	53.6 ± 6.9	83 ± 10.3	29.4	1.5
G395R	2850 ± 220	5995 ± 589	0.0001	8 ± 0.8	17.4 ± 2.4	9.4	2.1
F396C	11516 ± 725	15447 ± 607	0.0001	45.5 ± 2.6	61.5 ± 2.3	16.0	1.3
F396I	12835 ± 938	20028 ± 1684	0.0001	51.3 ± 4	80.2 ± 7.2	28.9	1.6
F396L	16519 ± 1148	29921 ± 1158	0.0001	65 ± 3.8	119.2 ± 4.7	54.3	1.8
F396V	20066 ± 1220	24860 ± 1682	0.0193	79.5 ± 4.6	99.3 ± 7.1	19.7	1.2
Y397C	4930 ± 944	11372 ± 1534	0.0001	18.4 ± 4.2	41.1 ± 7.1	22.7	2.3
Y397F	20498 ± 833	26411 ± 932	0.0001	71.3 ± 2.5	92.6 ± 3.8	21.3	1.3
Y397H	14821 ± 1007	21935 ±	0.0002	51.1 ± 2.4	76.7 ± 3.8	25.5	1.5

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
		1308					
Y397N	3438 ± 291	6232 ± 402	0.0001	13.5 ± 1	24.8 ± 1.7	11.4	1.8
Y397S	4624 ± 362	9056 ± 406	0.0001	16 ± 1	31.6 ± 1.4	15.7	2.0
E398G	12507 ± 771	15528 ± 885	0.0057	43.4 ± 2.3	54.9 ± 3.8	11.5	1.2
E398Q	22163 ± 1206	26967 ± 1243	0.0018	76.7 ± 3.2	94.4 ± 4.7	17.6	1.2
W399G	21476 ± 1276	28481 ± 1315	0.0007	74.8 ± 4.2	99.2 ± 4.3	24.3	1.3
W399R	15451 ± 1268	23299 ± 1725	0.0002	53.6 ± 3.9	81.2 ± 5.4	27.6	1.5
T400A	12742 ± 1056	26604 ± 1720	0.0001	41.8 ± 3.5	86.2 ± 5	44.4	2.1
T400I	8922 ± 851	14017 ± 1295	0.0001	28.3 ± 1.6	44 ± 2.2	15.7	1.6
T400N	21166 ± 1602	31312 ± 1522	0.0001	68.6 ± 4	103.1 ± 5.7	34.5	1.5
T400P	8423 ± 755	28286 ± 2670	0.0001	27.5 ± 2.1	89 ± 6.1	61.4	3.4
T400S	17855 ± 1480	27106 ± 1992	0.0004	59 ± 5.6	86.8 ± 5	27.8	1.5
S401A	18412 ± 2150	23425 ± 1714	0.0045	56.4 ± 3.2	74.9 ± 3.9	18.5	1.3
S401L	8799 ± 918	15148 ± 1020	0.0002	33.1 ± 3.6	57.3 ± 3.5	24.2	1.7
S401T	13582 ± 1242	23965 ± 1621	0.0001	43.3 ± 2.8	75.7 ± 3.9	32.4	1.8
R402G	19518 ± 1866	31224 ± 2455	0.0004	74.8 ± 8.3	121.1 ± 11.4	46.3	1.6
R402M	23649 ± 2051	33639 ± 1954	0.0013	87.4 ± 6.3	131.8 ± 10.8	44.4	1.4
R402S	25974 ± 2272	32424 ± 2592	0.0266	96.9 ± 8.1	128.7 ± 13.4	31.7	1.3
R402T	22606 ± 1743	30958 ± 2697	0.0083	81.4 ± 6.4	106.4 ± 4.9	25.0	1.4
R402W	14605 ± 1371	21501 ± 1053	0.0004	56.7 ± 6.4	83 ± 4.8	26.3	1.5
L403F	30710 ± 1843	37991 ± 1546	0.0004	91.4 ± 3.2	115 ± 4.6	23.6	1.2
L403V	26390 ± 767	32130 ± 807	0.0001	80.3 ± 3.2	98.8 ± 4.6	18.5	1.2
R404G	22301 ± 810	32168 ± 1138	0.0001	68.4 ± 3.3	98.7 ± 4.8	30.3	1.4
R404I	33222 ± 1740	44883 ± 3650	0.0015	99.7 ± 4.3	134.4 ± 9.5	34.7	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
R404K	30197 ± 1649	39268 ± 2115	0.0002	90.1 ± 3.4	118.5 ± 5.8	28.4	1.3
R404S	33060 ± 1443	42020 ± 2092	0.0002	100.3 ± 4.5	128 ± 6.9	27.7	1.3
R404T	28304 ± 1734	37173 ± 1791	0.0001	85 ± 4.5	112.7 ± 5.4	27.8	1.3
S405G	17071 ± 2013	21938 ± 1964	0.0158	49.4 ± 4.6	64.7 ± 4.6	15.3	1.3
H406D	36477 ± 2031	46168 ± 3080	0.0072	94.2 ± 3.9	118 ± 5.6	23.8	1.3
H406L	19135 ± 1127	23089 ± 1299	0.0283	81.5 ± 3.6	99.4 ± 5.2	17.9	1.2
H406Q	23925 ± 1238	30984 ± 1471	0.0007	99.3 ± 3.5	130.4 ± 6.2	31.1	1.3
I407L	9275 ± 775	14136 ± 1118	0.0009	37.8 ± 2.6	58.9 ± 4.7	21.1	1.5
I407M	6020 ± 370	12673 ± 641	0.0001	24.9 ± 1.2	53 ± 2.5	28.1	2.1
I407T	5565 ± 419	9751 ± 458	0.0001	23.1 ± 1.5	40.8 ± 1.7	17.7	1.8
N408D	15729 ± 571	23783 ± 870	0.0001	65.8 ± 1.8	99.8 ± 3.3	34.0	1.5
N408H	4294 ± 289	5224 ± 232	0.0042	17.8 ± 0.9	22 ± 1	4.2	1.2
N408T	25401 ± 1693	33264 ± 1531	0.0007	97.2 ± 6	129 ± 6.2	31.8	1.3
P409L	5691 ± 1184	11404 ± 1867	0.0007	19.9 ± 3.5	41.1 ± 5.2	21.2	2.0
T410S	13723 ± 1986	28944 ± 3416	0.0001	47.1 ± 6	99.1 ± 9.6	52.0	2.1
G411A	9911 ± 610	15641 ± 698	0.0001	34.3 ± 2.1	54.1 ± 2.3	19.8	1.6
G411C	9940 ± 492	13530 ± 529	0.0001	34 ± 1.3	46.6 ± 1.4	12.5	1.4
G411V	428 ± 38	4594 ± 128	0.0001	1.6 ± 0.2	16.2 ± 0.8	14.6	10.7
T412A	11226 ± 412	20104 ± 484	0.0001	39.5 ± 2.3	70.5 ± 3.1	31.0	1.8
T412I	4553 ± 335	13268 ± 538	0.0001	15 ± 0.9	44 ± 1.4	29.0	2.9
T412S	14822 ± 1059	20447 ± 906	0.0003	51.5 ± 4	70.4 ± 2.7	18.9	1.4
V413F	6626 ± 534	9755 ± 657	0.0013	21.6 ± 1.4	32 ± 1.6	10.3	1.5
V413G	1065 ± 60	2930 ± 303	0.0001	3.6 ± 0.2	9.5 ± 0.9	5.9	2.8
V413I	26821 ± 1450	33410 ± 2091	0.0014	93.8 ± 6.9	117.2 ± 9.7	23.3	1.3
L414F	16323 ± 958	25092 ± 844	0.0001	56.7 ± 3.5	87 ± 2.6	30.3	1.5
L414V	9522 ± 515	14805 ± 636	0.0001	31.4 ± 1.3	49.1 ± 1.7	17.7	1.6
L415H	11323 ± 474	14204 ± 528	0.0001	39.1 ± 1.3	49.2 ± 1.5	10.0	1.3
L415I	26954 ± 887	32699 ± 1144	0.0004	93.6 ± 3.1	113.1 ± 3	19.4	1.2

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
Q416E	22022 ± 886	27625 ± 1201	0.0009	76.4 ± 2.9	95.7 ± 3.9	19.3	1.3
Q416H	29518 ± 1787	41306 ± 2269	0.0001	96.6 ± 3.7	136.2 ± 6.1	39.7	1.4
Q416L	31088 ± 1385	38168 ± 1637	0.0024	107.5 ± 4.2	132.2 ± 5.4	24.7	1.2
L417I	29869 ± 2186	36566 ± 1460	0.0013	98.1 ± 5.4	122 ± 5	24.0	1.2
E418A	25155 ± 910	33780 ± 1103	0.0001	84.1 ± 3.2	112.8 ± 3.9	28.7	1.3
E418D	26797 ± 1152	32116 ± 1602	0.0096	79.6 ± 3.5	97.2 ± 6.5	17.5	1.2
E418K	10503 ± 452	16154 ± 633	0.0001	35.2 ± 1.7	54 ± 2.3	18.8	1.5
E418Q	25651 ± 1049	31249 ± 1099	0.0009	85.8 ± 3.6	103.9 ± 3.3	18.1	1.2
N419I	12161 ± 966	16825 ± 757	0.0001	36.1 ± 2.8	51 ± 3.3	14.9	1.4
N419S	26543 ± 1425	35911 ± 2777	0.0013	69.5 ± 3.6	93.3 ± 5.8	23.9	1.4
N419T	24406 ± 1544	35654 ± 2884	0.0001	64.6 ± 4.4	92.7 ± 6.3	28.2	1.5
N419Y	12788 ± 858	19160 ± 838	0.0001	37.9 ± 2.4	57.8 ± 3.3	19.9	1.5
T420K	20374 ± 1876	27866 ± 1129	0.0007	60.6 ± 3.8	86.6 ± 4.1	26.1	1.4
T420P	17155 ± 1546	26139 ± 851	0.0001	51.6 ± 3.4	82.1 ± 4.3	30.5	1.5
T420R	15732 ± 1356	26243 ± 771	0.0001	48.1 ± 3.4	82.4 ± 4.3	34.3	1.7
T420S	23505 ± 1306	32465 ± 897	0.0001	71.4 ± 2.6	101.5 ± 4.6	30.1	1.4
M421I	19000 ± 943	33949 ± 1412	0.0001	65.7 ± 2.5	118.9 ± 6	53.2	1.8
M421K	36942 ± 3086	45754 ± 1808	0.0004	123.9 ± 4.9	159.6 ± 6.2	35.7	1.2
M421L	21513 ± 1479	28263 ± 1128	0.0001	65.6 ± 3.4	87.5 ± 3.7	21.9	1.3
M421R	27913 ± 817	36429 ± 989	0.0001	87.1 ± 3.8	114.2 ± 5.5	27.1	1.3
M421T	14666 ± 828	21185 ± 707	0.0001	44.6 ± 1.8	66.2 ± 3.1	21.6	1.4
Q422P	27059 ± 2022	45170 ± 1440	0.0001	93.5 ± 5.9	157.3 ± 4.4	63.8	1.7
M423I	20857 ± 918	25268 ± 1106	0.0036	70.3 ± 3.6	85.8 ± 5.3	15.4	1.2
M423K	18352 ± 1047	24240 ± 993	0.0002	61.8 ± 3.8	81.4 ± 3.8	19.7	1.3
M423L	16037 ± 874	22114 ± 1324	0.0011	53.6 ± 2.8	73.3 ± 3.8	19.7	1.4

Table 7

α-Gal A Mutant Form	Baseline α-Gal A activity (nmol/mg/hr)	10 μM migalastat α-Gal A activity (nmol/mg/hr)	Mann-Whitney U p-value	Baseline α-Gal A activity (% WT)	10 μM migalastat α-Gal A activity (% WT)	Absolute increase (% WT)	Relative increase
M423T	19669 ± 956	26392 ± 1093	0.0001	66.1 ± 3.5	88.6 ± 4.2	22.5	1.3
S424L	27072 ± 1966	33333 ± 1634	0.0120	69.2 ± 4.7	88.1 ± 6.7	18.9	1.2
L425F	26370 ± 948	36447 ± 3394	0.0001	91.5 ± 4.6	125.1 ± 11.1	33.6	1.4
D427N	33454 ± 4593	49103 ± 5890	0.0249	82.4 ± 7.8	116.6 ± 7.7	34.2	1.5
L429R	29098 ± 1230	35876 ± 1241	0.0004	99.6 ± 5.3	123.3 ± 6	23.7	1.2

[00141] In Table 7, values for the mean ± standard error of the mean (SEM) were calculated. nmol/mg/hr indicates "nmoles of free 4-MU released per mg of protein per hour". WT indicates "wild-type". NC indicates "not calculable". N/A indicates "not applicable".

[00142] **Baseline and 10 μM migalastat α-Gal A activity:** Differences in the α-Gal A activity between lysates incubated in the absence and presence of 10 μM migalastat were determined using a one-tailed, Mann Whitney U test; an increase at 10 μM migalastat with a $p<0.05$ was considered significant. "BLD" indicates that the mean α-Gal A activity was below the limit of detection (<142 nmol/mg/hr).

[00143] **Baseline α-Gal A activity (% WT)** = (α-Gal A activity in mutant transfected cell lysates without migalastat ÷ α-Gal A activity in wild-type transfected cell lysates without migalastat) * 100.

[00144] **10 μM migalastat α-Gal A activity (% WT)** = (α-Gal A activity in mutant transfected cell lysates incubated with 10 μM migalastat ÷ α-Gal A activity in wild-type transfected cell lysates without migalastat) * 100.

[00145] **Absolute increase (% WT)** = is the 10 μM migalastat α-Gal A activity (% WT) minus the baseline α-Gal A activity (% WT).

[00146] **Relative increase** is the 10 μM migalastat α-Gal A activity in mutant transfected cell lysates ÷ baseline α-Gal A activity in mutant transfected cell lysates incubated without migalastat.

[00147] As can be seen from Table 7, the novel α-Gal A mutations listed in Table 2 demonstrated an *in vitro* response to incubation with migalastat that met amenability criteria.

Accordingly, patients with these mutations are expected to be treatable with migalastat therapy as described herein.

[00148] In some instances, a set of electronic components may communicate to determine a predicted result of using migalastat or a migalastat salt based on mutation data representing one or more mutations. The predicted result may be based on, for example, whether a mutation represented in the mutation data is identified in a data store and/or which data value(s) are associated with the identification in the data store.

[00149] FIG. 4 shows an exemplary interaction system 400 to generate treatment classifications based on mutation data. Depicted components (e.g. systems) may communicate with each other over one or more networks (e.g., the Internet, a wide-area network, a local-area network, the Internet or a short-range connection).

[00150] Interaction system 400 can include a provider system 405, which can be associated with a provider providing care to a subject. The provider may include (for example) a physician, nurse, health clinic, hospital, etc. The subject may include a person (e.g., male or female) diagnosed with or tentatively diagnosed with Fabry disease and/or diagnosed with or tentatively diagnosed with a disorder pertaining to α-Gal A activity. Provider system 405 may collect subject data corresponding to the data from a variety of sources. For example, some subject data may be locally collected as a result of information provided directly from the subject to the provider, such as demographic information, symptom profiles and/or treatment history. Some subject data may have been initially collected and/or detected at a laboratory system 410, such as urine-culture data (e.g., indicating whether any of proteinuria, albuminuria or accumulation of lyso-Gb3 were detected in a urine sample from the subject) and/or blood-test data (e.g., characterizing an activity of the α-galactosidase A enzyme and/or indicating whether an accumulation of Lyso-Gb3 was detected in a blood sample from the subject). Some subject data may have been collected by a sequencing system 415, which may sequence one or more genes and/or detect one or more mutations. For example, the GLA gene may be sequenced, and and a mutation-detection analysis may be performed to identify any mutation in the GLA gene (e.g., any single nucleotide polymorphism or structural mutation). Sequencing system 415 may identify and/or represent a mutation as a nucleotide mutation, protein sequence mutation, etc.

[00151] In some instances, provider system 405 sends subject-data requests (e.g., with an identifier of the subject) directly to laboratory system 410 and/or sequencing system 415,

potentially along with an indication that the subject has authorized availing data to the provider (e.g., the authorization being provided via a signature). In some instances, one or both of laboratory system 410 and sequencing system 415 transmit the subject data to a coordinating access control system 420, which controls a manages a central (e.g., remote and/or cloud-based) subject data store 425. Access control system 420 may perform data-aggregation, synchronization and authorization processes. For example, access control system 420 may use a white-list, black-list, cryptographic and//or account-verification technique to determine whether to update subject data store 425 based on data from a given system and/or whether to transmit requested data from subject data store 425 to a given system. To illustrate, access control system 420 may require use of a private information link (supported by a shared secret) between a provider system and the access control system in order to transmit any subject data to the provider system. As another example, a data synchronization process may – upon detecting inconsistent data – delete the older data value and use the newer data value, store each of the older and newer data values, assign a confidence to one or both of the older and newer data values (e.g., based on a reliability of a data source, degree to which the a data value is represented in a patient group), etc.

[00152] Provider system 405 can send a request to a mutation classification system 430 to generate a predictive metric or predictive output for the subject. The request can include or can be accompanied by at least some of the subject data, such as the sequence data (e.g., corresponding to one or more genes) and/or mutation data (e.g., corresponding to one or more genes).

[00153] The predictive metric and/or the predictive output may be predictive of whether and/or an extent to which a given treatment would be effective in treating, delaying and/or preventing a particular condition. For example, the predictive metric and/or predictive output may be predictive of whether and/or an extent to which administering migalastat or a migalastat salt (e.g., generally, in a particular dosage and/or via a particular route of administration) is effective at treating Fabry disease.

[00154] Mutation classifier system 430 can, in some instances, include a web server 432, at least one data processor 433 and a non-transitory computer readable storage medium 434. The web server 432 serves a webpage that accepts input that identifies mutation data. The webpage need not require entry of subject-identifying data. In some instances, the webpage may be configured such that the only input fields for accepting subject-associated data are to

accept sequence data and/or mutation data. In some instances, the webpage is configured such that a file that identifies a sequence can be uploaded. In some instances, the webpage is configured to include an input component that accepts text inputs that identify a mutation. The webpage may identify a format in which mutation identifications are to be represented and/or a file type to be used for sequence-data uploads.

[00155] Upon receiving a communication that corresponds to a request for a predictive metric and/or predictive output, mutation classifier system 430 can determine if an identification of a mutation (and/or if an uploaded sequence file) is of a correct format. In some embodiments, the determination of the proper format is made by data processor 433. For example, a format may require that a nucleotide mutation include a prefix letter ("c"), followed by a period (or these may be optional components). The format may further require that the mutation identify a wild-type nucleotide, the nucleotide number and a mutant nucleotide. The format may require (or permit) the ">" symbol and/or a particular order. For example, a permitted or required format may include the following components in the following order: (optionally "c.") nucleotide number, wild-type nucleotide, ">", and mutant nucleotide. As another example, a permitted or required forma may include the following components in the following order: (optionally "c."), wild-type nucleotide, nucleotide number and mutant nucleotide.

[00156] In some instances, if a mutation identification is not of a required or permitted format, mutation classifier system 430 may return an error indication by web server 432. In some instances, if a mutation identification provided in a first format is not of a required or permitted format, mutation classifier system 430 may generate one or more proposed identifications in a second format based on the input and transmit the proposed identification(s) to be availed at provider system 205 (e.g., presented at a webpage), such that one of the proposed identifications in the second format can be selected or such that the proposed identification(s) can guide subsequent input. The proposed identification(s) in the second format may be generated by data processor 433 by detecting numbers and/or letters in the initial input of the first format and reorganizing them in a manner that accords with a permitted or required format (e.g., and by adding or removing one or more characters, such as "." or ">"). In instances in which sequence data is received, mutation classifier system 430 can identify one or more mutations by comparing the sequence to a reference sequence.

[00157] Mutation classifier system 430 and data processor 433 can query an amenable mutation data store medium 435 using a representation of one or more mutations to retrieve data that corresponds to a predicted outcome of using each of one or more treatments by a subject having the one or more mutations. The outcome may relate to (for example) an efficacy and/or low incidence of adverse effects. The one or more treatments may include migalastat or a migalastat salt. The outcome can include or can be based on an observed outcome, such as one generated based on a human trial or animal experiment in which subjects having the mutation were administered the treatment, and their condition (e.g., state of a condition, such as state of Fabry disease) was monitored. The outcome can alternatively or additional include or can be based on a theoretical outcome, which may be based on in vitro experiments that indicate whether and/or an extent to which administering an agent corresponding to the treatment to cells having the mutation(s) has a target effect (e.g., increased α-Gal activity). In some instances, amenable mutation data store medium 435 indicates whether in vivo experiments/trials have been performed and analyzed (e.g., versus having only in vitro data or no data). In some instances, both in vivo and in vitro data is available for at least some of the mutations, and this paired data may be used to derive a scaling factor and/or transformation function to normalize data and/or transform in-vitro-based data to a different scale.

[00158] The data processor 433 can detect the query result from amenable mutation data store medium 435 and determine whether the query result indicates that the one or more mutations is amenable to a given treatment.

[00159] A result of a given query can include one or more of: an indication as to whether retrieved data corresponds to in vivo data or theoretical data (e.g., in-vitro-based data); an indication as to whether a treatment is predicted to be effective given an occurrence of an input-identified mutation; and/or a predicted magnitude (e.g., of efficacy, time course or adverse-event occurrence) of administering the treatment given an occurrence of an input-identified mutation. The indication as to whether a treatment is predicted to be effective may include a binary indicator. The binary indicator may be determined based on whether a magnitude of a desirable effect (as observed in an in vivo or in vitro study) exceeds a predefined magnitude threshold (e.g., such that median or mean values of treated and untreated data sets differ by at least 80%, 50%, 30%, 10% or 5%), whether a p value corresponding to the desirable effect is below a predefined p-value threshold (e.g.. 0.1, 0.05, 0.02, 0.01 or 0.005) and/or whether a confidence value corresponding to the desirable effect is below a predefined

confidence threshold (e.g., 70%, 80%, 90%, 95%, 98%, or 99%). The binary indicator may be determined based on whether a magnitude of an undesirable effect (as observed in an in vivo or in vitro study) is below a predefined magnitude threshold (e.g., such that median or mean values of treated and untreated data sets differ by less than 80%, 50%, 30%, 10% or 5%), whether a p value corresponding to the undesirable effect is above a predefined p-value threshold (e.g.. 0.1, 0.05, 0.02, 0.01 or 0.005) and/or whether a confidence value corresponding to the undesirable effect is above a predefined confidence threshold (e.g., 70%, 80%, 90%, 95%, 98%, or 99%). The predicted magnitude may correspond to subtractive or multiplicative differences between means or medians of the untreated and treated groups.

[00160] Further, the data processor 433 can generate output indicative of the amenability of the one more mutations to a given treatment. The output may be transmitted to and provided by the webserver 432 and/or the provider system 205.

[00161] In some instances, a request corresponds to multiple mutations. Amenable mutation data store medium 435 need not reliably include data corresponding to each possible mutation combination. Thus, mutation classifier system 430 and data processor 433 may separately retrieve data corresponding to each individual mutation. In some instances, mutation classifier system 430 and data processor 433 then selects data corresponding to a single mutation. The single mutation may correspond to (for example) a mutation from amongst the multiple mutations for which results were most positive (e.g., corresponding with metrics indicative of highest predicted efficacy and/or lowest predicted adverse-effect occurrence or magnitude), most negative, or at a midpoint. In some instances, rankings are assigned to individual mutations in amenable mutation data store medium 435, such that the single mutation is identified the mutation, and the single mutation is selected as that being of the lowest relative rank (with low ranks being superior to high ranks). Rankings may represent how predominant a mutation is in influencing a disease-treatment outcome.

[00162] In some instances, one or more classifications are assigned to each of one or more mutations and or to a collective mutation set (e.g., if multiple are identified in an input). For example, in some instances, amenable mutation data set 435 may identify one or more classifications for each represented mutation. A classification may correspond to (for example) a predicted efficacy magnitude, a prediction as to whether a treatment will result in any efficacy, a time scale of any efficacy, a predicted adverse-event magnitude and/or a prediction as to whether a treatment will result in any adverse events. In some instances, a classification

corresponds to transforming a numeric value of a single variable to a category of the same variable (using one or more thresholds). In some instances, a classification transforms values of multiple variables (e.g., corresponding to two or more of: predicted efficacy magnitude, predicted efficacy occurrence, predicted adverse-event magnitude and predicted adverse-event occurrence) to a single variable. Clustering-transformation functions may be defined based on (for example) clustering algorithms, component analyses (e.g., principal component analysis or independent component analysis), a neural network and/or user input. The classifications may be represented at amenable mutation data store medium 435 and/or determined by mutation classifier system 430. For example, amenable mutation data store medium 435 may associate each mutation with one or more classifications, or amenable mutation data store medium 435 may associate each mutation with one or more values (e.g., numeric values, binary values or even categorical values), which mutation classifier system 430 may process to identify the classification(s).

[00163] A data-store controller system 450 can control what data is included in amenable mutation data store medium 435. For example, data-store controller system 450 may authorize, receive and evaluate communications indicative of experimental results and/or study results from an in vivo study system 455 and/or in vitro testing system 460. The authorization process may include (for example) ensuring that the system is white-listed and/or has provided requisite authenticating information. In vivo study system 455 may be configured to (for example) assess data corresponding to a clinical trial (e.g., a Phase I, Phase II or Phase III trial) or corresponding to an experiment performed on a (human or non-human) animal. In some instances, authorization information may further be used to resolve any data conflict. For example, if multiple in vivo study systems 455 submit conflicting results as to whether a given treatment is effective (or an extent to which the given treatment is effective) when a particular mutation is detected, data-store controller system 450 may use a prioritization list to determine which of the in vivo study systems 455 is to control. Data conflicts may also be resolved so as to prioritize (for example) study data performed in accordance with clinical-trial procedures, performed on humans, performed on mammals and/or performed recently. In vitro testing system 460 may be configured to (for example) assess data corresponding to cell-culture experiments.

[00164] Upon receiving a result, provider system 405 may (but need not) further process the result in view of additional subject data (e.g., that is not related to genetic sequence data).

Based on the result (and any additional data), provider system 405 can identify an appropriate treatment strategy for the subject. The treatment may be selected as a treatment associated with a highest predicted (e.g., average, median or probability of) efficacy, lowest predicted (e.g., average, median or probability of) adverse-event incidence or combination thereof. In some instances, provider system 405 sends an order for a given treatment (e.g., prescription) to a pharmacy system 465. The subject or another entity may administer the treatment to the patient.

[00165] FIG. 5 illustrates an exemplary process for using mutation data to generate predictive metrics. Process 500 may be performed by (for example) mutation classifier system 430. Process 500 begins at block 505, at which a data set unit storing a data set is accessed that identifies, for each mutation of a set of mutations, a degree of responsiveness to a particular type of treatment. The degree of responsiveness may indicate (for example) a predicted efficacy magnitude, a predicted efficacy occurrence, a predicted adverse-event magnitude, and/or a predicted adverse-event occurrence. The type of treatment may include (for example) treatment with migalastat or migalastat salt. The degree of responsiveness may be constrained to a particular subject group (e.g., having a given condition and/or a mutation in a particular gene). The data set may have been derived from in vivo (e.g., human and/or non-human; primate and/or non-primate; mammal and/or non-mammal) studies and/or in vitro studies. The data set may be accessed from one or more local or remote data stores.

[00166] At block 510, a communication is received that identifies one or more particular mutations. For example, the particular mutations(s) may include one or more nucleotide mutations and/or one or more protein mutations. The particular mutation(s) may correspond to one or more genes. The communication may be received over a network and may have been generated in response to provision of input at a webpage. The particular mutation(s) may correspond to a particular subject and may have been identified based on (for example) input from the subject, from a provider and/or from a sequencing system.

[00167] At block 515, a data set is queried using a representation of the one or more particular mutations. The data set may be local or remote to a computer system performing the query. The query may correspond to a request for data indicating an effect of administration of a particular treatment to a subject having (one, some or all) of the particular mutation(s). The query may (but need not specify) the particular treatment.

[00168] The data set may include or may be based on experimental data that indicates whether or an extent to which the particular treatment increases α-Gal A activity. More specifically, α-Gal A activity (e.g., a mean or median activity) may be determined for wild-type cells; each of a set of mutant cells, and each of a set of treated mutant cells (having been treated with the particular treatment). The data set may include each of these values. The data set may include, for each of a set of mutations, a fraction or percentage that compares the α-Gal activity of mutant cells (having the mutation) to the α-Gal activity of the wild-type cells and/or a fraction or percentage that compares the α-Gal activity of treated mutant cells to the α-Gal activity of the wild-type cells.

[00169] The data set may include, for each of the set of mutations, an absolute difference between the α-Gal activity of the treated mutant cells and the α-Gal activity of untreated mutant cells and/or an absolute difference between the relative α-Gal activity of the treated mutant cells (as compared to wild-type instances) and the relative α-Gal activity of the untreated mutant cells. The data set may include, for each of the set of mutations, a relative difference calculated by subtracting the α-Gal activity of untreated mutant cells from the α-Gal activity of treated mutant cells or by subtracting the relative α-Gal activity of untreated mutant cells (relative to wild-[type instances) from the relative α-Gal activity of treated mutant cells.

[00170] The data set may include, for each of the set of mutations, a category or binary indicator determined based on one of the aforementioned activity values, For example, an activity-change variable Δ may be defined as: $activity_{treated,mutant}/activity_{WT} - activity_{untreated,mutant}/activity_{WT}$, where *activity* is α-Gal activity. Categories may be defined as: $\Delta \leq 1$, $1 < \Delta \leq 5$, $5 < \Delta \leq 10$, $10 < \Delta \leq 20$, and $20 < \Delta$. As another example, a binary indicator can be set to "Amenable" when $\Delta > thresh$ and "Unamenable" when $\Delta \leq thresh$ (e.g., where thresh is set to 1.0, 2.0, 5.0, or 10.0).

[00171] As another example, an activity-change variable Δ may be defined as: $100\% * activity_{treated,mutant} / activity_{untreated,mutan}$. Categories may be defined as: $\Delta \leq 100\%$, $100\% < \Delta \leq 105\%$, $105\% < \Delta \leq 110\%$, $110\% < \Delta \leq 150\%$, and $150\% < \Delta$. As another example, a binary indicator can be set to "Amenable" when $\Delta > thresh$ and "Unamenable" when $\Delta \leq thresh$ (e.g., where thresh is set to 100%, 101%, 105% or 110%.

[00172] At block 520, one or more results for the query may be detected. The query result(s) may indicate a degree to which a subject having the particular mutation is amenable to

each of one or more treatments (e.g., migalastat and/or a migalastat salt). The query result(s) may indicate a predicted occurrence of and/or magnitude of an efficacy and/or adverse-event incidence of administering the treatment. The query result(s) may include a binary indication (e.g., indicating whether each of the particular mutation(s) is amenable to the particular treatment(s)) and/or a numeric or categorical value that more specifically indicates a degree to which each of the particular mutation(s) is amenable to the particular treatment(s).

[00173] In some instances, the query result identifies an α-Gal A activity metric associated with mutant, treated cells; mutant, untreated cells; and/or wild-type cells and/or absolute or relative differences between two or more of such cell types.

[00174] At block 525, a metric is determined corresponds to a predicted effect of administering a treatment (e.g., an identified particular treatment) to a subject having the particular mutation(s). The metric may include one or more query results and/or processed version(s) thereof. For example, a relative or absolute difference can be calculated between α-Gal A activity in treated mutant cells as compared to as in untreated mutant cells (e.g., with the activity being an absolute value or relative to wild-type activity). Further, a numeric result (or processed version thereof) can be converted into a categorical or binary metric. Further, if multiple particular mutations are identified, the metric may be a maximum, minimum, average or median of mutation-specific results. The metric may include a predicted occurrence of and/or magnitude of an efficacy and/or adverse-event incidence of administering the treatment.

[00175] At block 530, the metric is output. Outputting the metric may include (for example) transmitting the metric to a provider system or subject device, such that it is displayed via an interface at the provider system or subject device. Alternatively or additionally, outputting the metric can include locally presenting and/or storing the metric (e.g., in association with an identifier of the subject and/or of the particular mutation(s).

[00176] In some instances, the metric itself indicates and/or is accompanied by an indication as to whether the metric was based on theoretical and/or in vitro data. For example, a metric generated based on in vivo human data that indicates that a treatment is effective for treating a given condition in relation to a given mutation may be differentially represented from a metric generated based only on in vitro or simulation data that indicates a similar efficacy in a similar context. Thus, in some instances, four potential metrics are available: Amenable for treatment based on in vivo data; unamenable for treatment based on in vivo data; amenable for treatment based on in vitro data; and unamenable for treatment based on in vitro

data. In some instances, a variable type differs between instances supported by in vivo data and other instances. For example, the metric may be a binary indicator when supported by in vivo data but may be a categorical or numeric value in other instances.

[00177] FIG. 6 illustrates an exemplary process for using mutation data to generate predictive outputs. Process 600 may be performed by (for example) mutation classifier system 430, including webserver 432, data processor 433 and storage medium 434. Process 600 begins at block 605, at which an electronic communication is received by the webserver 432 that corresponds to an identification of one or more particular mutations. The communication may be received as (for example) an HTTP request received in correspondence with a webpage. The particular mutation(s) may (but need not) correspond to one or more particular genes.

[00178] At block 610, an amenable-mutation data store is queried by the data processor 433 using the particular mutation identification(s).The amenable mutation data store may local or remote relative to a computer system transmitting the query. The query may correspond to a request for data indicating an effect of administration of a particular treatment to a subject having (one, some or all) of the particular mutation(s). The query may (but need not specify) the particular treatment. The amenable-mutation data store medium 435 may include one or more types of data and/or characteristics as described in relation to the data set queried at block 500 in process 500.

[00179] In some instances, the amenable-mutation data store medium 435 selectively lists and/or stores data for mutations determined to be amenable for a given treatment (e.g., migalastat or a migalastat salt). For example, mutations may be selectively identified for inclusion in the amenable-mutation data store when in vivo data indicates that the treatment is effective when the mutation is present and/or when in vitro data indicates that administering the treatment to cells having the mutation results in a desired effect (e.g., increasing absolute α-Gal A activity by at least a threshold amount as compared to untreated instances or increasing α-Gal A activity, relative to wild-type instances, by at least a threshold amount as compared to untreated mutant instances).

[00180] At block 615, one or more results for the query may be detected by the data processor 433. The query result(s) may indicate whether the particular mutation (or each of multiple identifier particular mutations) is amenable to the particular treatment. The query result may indicate whether the particular mutation was represented in the amenable-mutation data store, and/or the query result may include one or more values associated with an identifier

of the particular mutation in the amenable-mutation data store (e.g., indicating an effect of the treatment when the particular treatment is administered and/or indicating a type of experiment or study used to identify such effect).

[00181] At block 620, one or more outputs indicative of a suitability of one or more treatments, with respect to a subject having the particular mutation(s), are generated by the data processor 433. The output(s) can include or can be generated based on the query result(s). For example, if multiple particular mutations are being assessed, the output(s) may include a query result for each of the particular mutations or a maximum, average, median or minimum result. To illustrate, the output may indicate that multiple particular mutations are collectively amenable to a treatment if query results indicate that at least one of the particular mutations is individually amenable to the treatment. The output may be numeric, binary, and/or categorical. The output(s) may be numeric, categorical or binary. In some instances, a numeric and/or categorical input represents increased suitability as a predicted occurrence and/or predicted magnitude of an effect increases and/or as a predicted occurrence and/or predicted magnitude of an adverse event increases.

[00182] At block 625, the output is transmitted by the data processor 433 to the webserver 432 or the provider system 205. For example, the output can be transmitted to a provider system or subject device, such that it is displayed via an interface at the provider system or subject device.

[00183] FIG. 7 illustrates exemplary mutation representations for to be used to facilitate assessments of mutation-based effects. For example, two different formats for representing nucleotide mutations are represented. Each includes the wild-type amino acid (first amino acid) and mutant amino acid (second amino acid), as well as the amino acid position. Thus, detecting whether a given character or character string corresponds to a letter, number, multi-digit number, etc. can indicate which (if any) of the above fields are represented by the character or character string. This determination can facilitate automated or suggested transformation of mutation format. The third column represents a representation of various protein sequence mutations, which further convey wild-type and mutant proteins and positio

[00184] FIG. 8 illustrates an exemplary interface to facilitate mutation-based treatment classifications. The depicted interface provides information that indicates formats in which mutations are to be identified. In the depicted instance, the searched mutation does not comply with the format. A returned result suggests multiple mutation representations that may

correspond to the input. The methods, systems, and devices discussed above are examples. Various configurations may omit, substitute, or add various procedures or components as appropriate. For instance, in alternative configurations, the methods may be performed in an order different from that described, and/or various stages may be added, omitted, and/or combined. Also, features described with respect to certain configurations may be combined in various other configurations. Different aspects and elements of the configurations may be combined in a similar manner. Also, technology evolves and, thus, many of the elements are examples and do not limit the scope of the disclosure or claims.

[00185] Specific details are given in the description to provide a thorough understanding of exemplary configurations including implementations. However, configurations may be practiced without these specific details. For example, well-known circuits, processes, algorithms, structures, and techniques have been shown without unnecessary detail in order to avoid obscuring the configurations. This description provides example configurations only, and does not limit the scope, applicability, or configurations of the claims. Rather, the preceding description of the configurations will provide those skilled in the art with an enabling description for implementing described techniques. Various changes may be made in the function and arrangement of elements without departing from the spirit or scope of the disclosure.

[00186] Also, configurations may be described as a process which is depicted as a schematic flowchart or block diagram. Although each may describe the operations as a sequential process, many of the operations can be performed in parallel or concurrently. In addition, the order of the operations may be rearranged. A process may have additional operations not included in the figure. Furthermore, examples of the methods may be implemented by hardware, software, firmware, middleware, microcode, hardware description languages, or any combination thereof. When implemented in software, firmware, middleware, or microcode, the program code or code segments to perform the necessary tasks may be stored in a non-transitory computer-readable medium such as a storage medium. Processors may perform the described tasks.

[00187] Having described several example configurations, various modifications, alternative constructions, and equivalents may be used without departing from the spirit of the disclosure. For example, the above elements may be components of a larger system, wherein other rules may take precedence over or otherwise modify the application of the technology.

Also, a number of operations may be undertaken before, during, or after the above elements are considered. Accordingly, the above description does not bind the scope of the claims.

[00188] As used herein and in the appended claims, the singular forms "a", "an", and "the" include plural references unless the context clearly dictates otherwise. Thus, for example, reference to "a user" includes a plurality of such users, and reference to "the processor" includes reference to one or more processors and equivalents thereof known to those skilled in the art, and so forth.

[00189] Also, the words "comprise", "comprising", "contains", "containing", "include", "including", and "includes", when used in this specification and in the following claims, are intended to specify the presence of stated features, integers, components, or operations, but they do not preclude the presence or addition of one or more other features, integers, components, operations, acts, or groups.

[00190] The patent and scientific literature referred to herein establishes the knowledge that is available to those with skill in the art. All United States patents and published or unpublished United States patent applications cited herein are incorporated by reference. All published foreign patents and patent applications cited herein are hereby incorporated by reference. All other published references, documents, manuscripts and scientific literature cited herein are hereby incorporated by reference.

[00191] While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.

What is claimed is:

1. A method of treating Fabry disease in a subject comprising:

accessing mutation information corresponding to the subject, the mutation information identifying one or more α-galactosidase A mutations;

determining, based on the mutation information, that the subject has at least one mutation as identified in Table 2; and

administering migalastat or a salt thereof to the subject determined to have at least one mutation as identified in Table 2.

2. The method of claim 1, wherein determining that the subject has at least one mutation as identified in Table 2 includes:

initiating a query of a data store that identifies two or more mutations from a set of mutations identified in Table 2; and

receiving a query result that identifies the at least one mutation is represented in the mutation information and also in Table 2.

3. The method of claim 2, wherein the data store further identifies two or more mutations from another set of mutations identified in Table 1.

4. The method of claim 2 or 3, wherein the data store includes at least 50% of the set of mutations identified in Table 2.

5. The method of any of claims 2-4, wherein the query is initiated by accessing a particular webpage hosted by a web server that controls a data store identifying at least some of the mutations in Table 2.

6. The method of any of claims 2-4, wherein the query is initiated by:

accessing a particular webpage on a website;

providing input at the particular webpage that identifies at least part of the mutation information; and

selecting an option at the webpage to submit, to a web server, an electronic request to perform the query, the electronic request including a representation of the input;

wherein the query result is received from the web server in response to the query and is displayed at the particular webpage or another webpage on the website.

7. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues 5-14, 17-18, 20-30, 32-33, 36-39, 41, 43, 45-46, 48, 50-51, 53-56, 58-62, 64-89, 91, 96-99, 101-102, 104-110, 113-117, 121, 123-131, 133, 135-141, 143-153, 156-162, 164-167, 169, 171, 173, 175-178, 180-182, 184-201, 203, 204, 206-222, 224, 227- 230, 232-233, 235, 237-261, 263-265, 267-270, 272-273, 275, 277-278, 280-286, 288-289, 291-292, 294-295, 297-300, 302-304, 306-322, 324-327, 329-339, 341, 343-344, 346-357, 359, 362-371, 373- 377, 379-381, 383-388, 391-425, 427, 429, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

8. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues -14, 17-18, 20-30, 32-33, 36-39, 41, 43, 45-46, 48, 50-51, 53-56, 58-62, 64-89, 91, 96-99, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

9. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues 101-102, 104-110, 113-117, 121, 123-131, 133, 135-141, 143-153, 156-162, 164-167, 169, 171, 173, 175-178, 180-182, 184-201, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

10. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues 203, 204, 206-222, 224, 227- 230, 232-233, 235, 237-261, 263-265, 267-270, 272-273, 275, 277-278, 280-286, 288-289, 291-292, 294-295, 297-300, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

11. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues 302-304, 306-322, 324-327, 329-339, 341, 343-344, 346-357, 359, 362-371, 373- 377, 379-381, 383-388, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

12. The method of any of claims 1-6, wherein the at least one mutation includes one or more mutations of α-galactosidase A at amino acid residues 391-425, 427, 429, or any combination thereof, wherein the residues are numbered relative to SEQ ID NO:2.

13. The method of any of claims 1-12, wherein the at least one mutation includes a mutation:
at amino acid residue 5 that comprises N5D or N5K;
at amino acid residue 6 that comprises P6L, P6Q, P6R, P6S, or P6T;
at amino acid residue 7 that comprises E7D, E7K, E7V;
at amino acid residue 8 that comprises, L8I, L8P, L8Q;
at amino acid residue 9 that comprises H9L, H9Q, H9R, or H9Y;
at amino acid residue 10 that comprises, L10M, L10P, L10Q,, L10R, or L10V;
at amino acid residue 11 that comprises G11C, G11D, G11R, G11S, or G11V;
at amino acid residue 12 that comprises C12G, C12R, C12S, or C12Y;
at amino acid residue 13 that comprises A13E or A13G;
at amino acid residue 14 that comprises L14F, L14H, or L14V
at amino acid residue 17 that comprises R17C, R17G, R17H, R17P, or R17S;
at amino acid residue 18 that comprises, F18I or F18L;
at amino acid residue 20 that comprises A20G;
at amino acid residue 21 that comprises L21H;
at amino acid residue 22 that comprises V22A, V22F, V22I, or V22L;
at amino acid residue 23 that comprises S23P orS23T;
at amino acid residue 24 that comprises W24S; or
at amino acid residue 25 that comprises D25H;
wherein the residues are numbered relative to SEQ ID NO:2.

14. The method of any of claims 1-13, wherein the at least one mutation includes a mutation:
at amino acid residue 26 that comprises I26N;

at amino acid residue 27 that comprises P27A, P27L, P27S, or P27T;
at amino acid residue 28 that comprises G28E, G28R or G28W;
at amino acid residue 29 that comprises A29G, A29P, or A29V;
at amino acid residue 30 that comprises R30G
at amino acid residue 32 that comprises L32M, L32Q, L32R, or L32V;
at amino acid residue 33 that comprises D33A, D33E, or D33V;
at amino acid residue 36 that comprises L36M or L36V;
at amino acid residue 37 that comprises A37E, A37G, or A37S;
at amino acid residue 38 that comprises R38G, R38M, or, R38W;
at amino acid residue 39 that comprises, T39A, T39K, T39M, T39R, or T39S;
at amino acid residue 41 that comprises T41A, T41N, or T41S;
at amino acid residue 43 that comprises G43A;
at amino acid residue 45 that comprises L45M or L45V;
at amino acid residue 46 that comprises H46D, H46N, or H46Q;
at amino acid residue 48 that comprises E48A; or
at amino acid residue 50 that comprises F50Y;
wherein the residues are numbered relative to SEQ ID NO:2.

15. The method of any of claims 1-14, wherein the at least one mutation includes a mutation:
at amino acid residue 51 that comprises M51R, M51T, or M51V;
at amino acid residue 53 that comprises N53H;, N53I, N53S, or N53T;
at amino acid residue 54 that comprises L54H, L54R, or L54V;
at amino acid residue 55 that comprises D55A, D55E, D55H, or D55Y;
at amino acid residue 56 that comprises C56W;
at amino acid residue 58 that comprises E58K;
at amino acid residue 59 that comprises E59A, E59D, E59G, E59Q, or E59V;
at amino acid residue 60 that comprises P60A, P60Q, or P60R;
at amino acid residue 61 that comprises D61E, or D61V;
at amino acid residue 62 that comprises S62A, S62C, S62F, S62P, or S62Y;
at amino acid residue 64 that comprises I64L, or I64V;
at amino acid residue 65 that comprises S65C, S65G, or S65R;
at amino acid residue 66 that comprises E66D or E66V;

at amino acid residue 67 that comprises K67E, K67M, K67N, K67Q, or K67T;
at amino acid residue 68 that comprises L68I;
at amino acid residue 69 that comprises F69I or F69Y;
at amino acid residue 70 that comprises M70I,, M70K, M70L, or M70R;
at amino acid residue 71 that comprises E71A, E71D, E71G, E71Q, or E71V;
at amino acid residue 72 that comprises M72L or M72T;
at amino acid residue 73 that comprises A73S or A73T;
at amino acid residue 74 that comprises, E74D, E74G, E74K, or E74V; or
at amino acid residue 75 that comprises L75F or L75P;
wherein the residues are numbered relative to SEQ ID NO:2.

16. The method of any of claims 1-15, wherein the at least one mutation includes a mutation:
at amino acid residue 76 that comprises M76V;
at amino acid residue 77 that comprises V77I orV77L;
at amino acid residue 78 that comprises S78L or S78P;
at amino acid residue 79 that comprises E79A, E79D, E79G, E79K, E79Q, or E79V;
at amino acid residue 80 that comprises G80A, G80C, or G80S;
at amino acid residue 81 that comprises W81L;
at amino acid residue 82 that comprises K82E, K82M, K82N, K82R, or K82T;
at amino acid residue 83 that comprises D83A, D83E, D83G, or D83V;
at amino acid residue 84 that comprises A84E, A84G, A84P, A84S, A84T, or A84V;
at amino acid residue 85 that comprises G85A, G85C, or G85R;
at amino acid residue 86 that comprises Y86F;
at amino acid residue 87 that comprises E87G;
at amino acid residue 88 that comprises Y88H, or Y88N;
at amino acid residue 89 that comprises L89V
at amino acid residue 91 that comprises I91F, I91L, I91M, or I91S;
at amino acid residue 96 that comprises M96L orM96T;
at amino acid residue 97 that comprises A97D, A97S, or A97T;
at amino acid residue 98 that comprises P98H, P98L, or P98R; or
at amino acid residue 99 that comprises Q99E, Q99L, Q99P, or Q99R;
wherein the residues are numbered relative to SEQ ID NO:2.

17. The method of any of claims 1-16, wherein the at least one mutation includes a mutation:
at amino acid residue 101 that comprises D101A, D101E, D101G, D101H, D101V;
at amino acid residue 102 that comprises S102A, S102P, or S102T;
at amino acid residue 104 that comprises G104A, G104D, or G104S;
at amino acid residue 105 that comprises R105G, R105I, R105K, or R105T
at amino acid residue 106 that comprises L106H, L106I, L106P, or L106V;
at amino acid residue 107 that comprises Q107E, Q107H, or Q107K;
at amino acid residue 108 that comprises A108E or A108V;
at amino acid residue 109 that comprises D109A, D109E, D109H, D109N, or D109Y;
at amino acid residue 110 that comprises P110T;
at amino acid residue 113 that comprises F113V, or F113Y;
at amino acid residue 114 that comprises P114L;
at amino acid residue 115 that comprises H115D or H115N;
at amino acid residue 116 that comprises G116R;
at amino acid residue 117 that comprises I117M or I117T;
at amino acid residue 121 that comprises A121V;
at amino acid residue 123 that comprises Y123D, Y123F, Y123N, or Y123S;
at amino acid residue 124 that comprises V124I; or
at amino acid residue 125 that comprises H125D, H125N, or H125R;
wherein the residues are numbered relative to SEQ ID NO:2.

18. The method of any of claims 1-17, wherein the at least one mutation includes a mutation:
at amino acid residue 126 that comprises S126C or S126I,;
at amino acid residue 127 that comprises K127E;
at amino acid residue 128 that comprises G128A;
at amino acid residue 129 that comprises L129V;
at amino acid residue 130 that comprises K130M, K130N, or K130Q;
at amino acid residue 131 that comprises L131V;
at amino acid residue 133 that comprises, I133L, I133T, or I133V;
at amino acid residue 135 that comprises A135E, A135G, A135S, or A135T;
at amino acid residue 136 that comprises D136A, D136N or D136V;

at amino acid residue 137 that comprises V137A, V137D, V137G, V137I or V137L;
at amino acid residue 138 that comprises G138A;
at amino acid residue 139 that comprises N139H N139I, N139K, or N139Y;
at amino acid residue 140 that comprises K140E, K140I, K140N, K140Q, or K140R;
at amino acid residue 141 that comprises T141S;
at amino acid residue 143 that comprises, A143E, or A143G;
at amino acid residue 144 that comprises G144A, G144C, G144R, or G144S;
at amino acid residue 145 that comprises F145C, F145L, F145V or F145Y;
at amino acid residue 146 that comprises P146A, P146H, P146L, or P146T;
at amino acid residue 147 that comprises G147A;
at amino acid residue 148 that comprises S148C, S148G, or S148T;
at amino acid residue 149 that comprises F149C; or
at amino acid residue 150 that comprises G150E or G150V;
wherein the residues are numbered relative to SEQ ID NO:2.

19. The method of any of claims 1-18, wherein the at least one mutation includes a mutation:
at amino acid residue 151 that comprises Y151C, Y151D, or Y151S
at amino acid residue 152 that comprises Y152F, or Y152S;
at amino acid residue 153 that comprises D153A, D153H, D153N D153V, or D153Y;
at amino acid residue 156 that comprises A156G;
at amino acid residue 157 that comprises Q157E, Q157K, Q157L, or Q157P;
at amino acid residue 158 that comprises T158A, T158I, T158N, or T158S;
at amino acid residue 159 that comprises F159I, F159L, F159V, or F159Y;
at amino acid residue 160 that comprises A160G, A160S, A160T or A160V;
at amino acid residue 161 that comprises D161H, D161N, D161V, or D161Y;
at amino acid residue 162 that comprises W162S;
at amino acid residue 164 that comprises V164A, V164I, or V164L;
at amino acid residue 165 that comprises D165A or D165E;
at amino acid residue 166 that comprises L166M or L166Q;
at amino acid residue 167 that comprises L167I;
at amino acid residue 169 that comprises F169C, F169L, F169V, or F169Y;
at amino acid residue 171 that comprises G171A or G171V;

at amino acid residue 173 that comprises Y173C, Y173F, Y173H, or Y173S; or
at amino acid residue 175 that comprises D175G, D175H, D175V, or D175Y;
wherein the residues are numbered relative to SEQ ID NO:2.

20. The method of any of claims 1-19, wherein the at least one mutation includes a mutation:
at amino acid residue 176 that comprises S176C or S176R;
at amino acid residue 177 that comprises L177F, L177M, L177S, L177V, or L177W;
at amino acid residue 178 that comprises E178A, E178G, E178K, or E178Q;
at amino acid residue 180 that comprises L180M, or L180S;
at amino acid residue 181 that comprises A181P, A181T, or A181V
at amino acid residue 182 that comprises D182A, D182E, D182V, or D182Y;
at amino acid residue 184 that comprises Y184F, Y184H, or Y184S;
at amino acid residue 185 that comprises K185M, K185N, K185Q, or K185T ;
at amino acid residue 186 that comprises H186D, H186L, H186N, H186Q, or H186Y;
at amino acid residue 187 that comprises M187L;
at amino acid residue 188 that comprises S188A, S188C S188F, S188P, S188T, or S188Y;
at amino acid residue 189 that comprises L189S or L189V;
at amino acid residue 190 that comprises A190D, A190G, A190S, A190T, or A190V;
at amino acid residue 191 that comprises L191M or L191V;
at amino acid residue 192 that comprises N192D, N192H, N192K, N192S, or N192T;
at amino acid residue 193 that comprises R193G, R193M, R193T or R193W;
at amino acid residue 194 that comprises T194N, T194P, or T194S;
at amino acid residue 195 that comprises G195C, G195R, or G195S;
at amino acid residue 196 that comprises R196I,or R196K;
at amino acid residue 197 that comprises S197C, S197G, S197I, S197N, or S197T;
at amino acid residue 198 that comprises I198M or I198S;
at amino acid residue 199 that comprises V199E or V199L; or
at amino acid residue 200 that comprises Y200N or Y200S;
wherein the residues are numbered relative to SEQ ID NO:2.

21. The method of any of claims 1-20, wherein the at least one mutation includes a mutation:

at amino acid residue 201 that comprises S201A, S201C, or S201T;

at amino acid residue 203 that comprises E203A, E203G, or E203Q;

at amino acid residue 204 that comprises W204S;

at amino acid residue 206 that comprises L206F, L206H, L206I, L206R, or L206V;

at amino acid residue 207 that comprises Y207F;

at amino acid residue 208 that comprises M208K;

at amino acid residue 209 that comprises W209C, or W209G;

at amino acid residue 210 that comprises P210H or P210T;

at amino acid residue 211 that comprises F211C, F211L, F211S, F211V, or F211Y;

at amino acid residue 212 that comprises Q212H, or Q212P;

at amino acid residue 213 that comprises K213E, or K213Q;

at amino acid residue 214 that comprises P214A, P214H, P214R, or P214T;

at amino acid residue 215 that comprises N215H, N215K, N215T, or N215Y;

at amino acid residue 216 that comprises Y216F, Y216H, , or Y216N;

at amino acid residue 217 that comprises T217A, T217I, T217K, T217P, T217R, or T217S;

at amino acid residue 218 that comprises E218A, E218D, E218G, E218K, E218Q, or E218V

at amino acid residue 219 that comprises I219F, I219M, or I219S;

at amino acid residue 220 that comprises R220L;

at amino acid residue 221 that comprises Q221E, Q221H, Q221K.,Q221L, or Q221R

at amino acid residue 222 that comprises Y222C, Y222D, Y222H, Y222N, or Y222S; or

at amino acid residue 224 that comprises N224H;

wherein the residues are numbered relative to SEQ ID NO:2.

22. The method of any of claims 1-21, wherein the at least one mutation includes a mutation:

at amino acid residue 227 that comprises R227G;

at amino acid residue 228 that comprises N228H, N228I, or N228T;

at amino acid residue 229 that comprises F229I, F229S, or F229Y;

at amino acid residue 230 that comprises A230D, A230G, A230P, or A230V;

at amino acid residue 232 that comprises I232L, I232M, or I232V;

at amino acid residue 5 that comprises D233A, D233E, D233G, or D233V;
at amino acid residue 235 that comprises S235A or S235T;
at amino acid residue 237 that comprises K237I;
at amino acid residue 238 that comprises S238C, S238I, or S238T;
at amino acid residue 239 that comprises I239L;
at amino acid residue 240 that comprises K240E, K240M, or K240R;
at amino acid residue 241 that comprises S241C, S241I, or S241T;
at amino acid residue 242 that comprises I242L, I242M, or I242S;
at amino acid residue 243 that comprises L243M, L243S, or L243V;
at amino acid residue 244 that comprises D244A, D244E, D244G, D244V, or D244Y;
at amino acid residue 245 that comprises W245C,
at amino acid residue 246 that comprises T246A, T246I, T246K, or T246R;
at amino acid residue 247 that comprises S247A, S247F, S247T, or S247Y;
at amino acid residue 248 that comprises F248C, F248L, F248V, or F248Y;
at amino acid residue 249 that comprises N249D, N249H, N249I, N249S, N249T, or N249Y;
at amino acid residue 250 that comprises Q250E or Q250L;
wherein the residues are numbered relative to SEQ ID NO:2.

23. The method of any of claims 1-22, wherein the at least one mutation includes a mutation:
at amino acid residue 251 that comprises E251G, E251K, E251Q, or E251V;
at amino acid residue 252 that comprises R252G;
at amino acid residue 253 that comprises I253F, I253N, or I253V;
at amino acid residue 254 that comprises V254A, V254D, V254F, or V254G;
at amino acid residue 255 that comprises D255A. D255E, D255H, D255N, D255V, or D255Y;
at amino acid residue 256 that comprises V256D, V256G, or V256L;
at amino acid residue 257 that comprises A257S;
at amino acid residue 258 that comprises G258E;
at amino acid residue 259 that comprises P259A, or P259T;
at amino acid residue 260 that comprises G260W;
at amino acid residue 261 that comprises G261A;

at amino acid residue 263 that comprises N263H or N263T;
at amino acid residue 264 that comprises D264H or D264N;
at amino acid residue 265 that comprises P265A or P265Q;
at amino acid residue 267 that comprises M267L or M267V;
at amino acid residue 268 that comprises L268F or L268I;
at amino acid residue 269 that comprises V269L;
at amino acid residue 270 that comprises I270L, I270S, or I270V;
at amino acid residue 272 that comprises N272D;
at amino acid residue 273 that comprises F273Y; or
at amino acid residue 275 that comprises L275I;
wherein the residues are numbered relative to SEQ ID NO:2.

24. The method of any of claims 1-23, wherein the at least one mutation includes a mutation:
at amino acid residue 277 that comprises W277L;
at amino acid residue 278 that comprises N278I,;
at amino acid residue 280 that comprises Q280L or Q280R;
at amino acid residue 281 that comprises V281A, V281E, , V281G, or V281L
at amino acid residue 282 that comprises T282S;
at amino acid residue 283 that comprises Q283E, Q283H, or Q283L;
at amino acid residue 284 that comprises M284I or M284L;
at amino acid residue 285 that comprises A285G, A285T, or A285V;
at amino acid residue 286 that comprises L286F, L286H, or L286V;
at amino acid residue 288 that comprises A288G, A288S, or A288V;
at amino acid residue 289 that comprises I289L, I289T or I289V;
at amino acid residue 291 that comprises A291G;
at amino acid residue 292 that comprises A292G or A292S;
at amino acid residue 294 that comprises L294F, L294I, or L294V
at amino acid residue 295 that comprises F295I, F295S, F295V, or F295Y,;
at amino acid residue 297 that comprises S297T;
at amino acid residue 298 that comprises N298D, N298I, or N298T;
at amino acid residue 299 that comprises D299H or D299N; or
at amino acid residue 300 that comprises L300I or L300V;

wherein the residues are numbered relative to SEQ ID NO:2.

25. The method of any of claims 1-24, wherein the at least one mutation includes a mutation:

at amino acid residue 302 that comprises H302D, H302L, H302N, or H302Y;

at amino acid residue 303 that comprises I303S;

at amino acid residue 304 that comprises S304I;

at amino acid residue 306 that comprises Q306E, Q306L, or Q306P;

at amino acid residue 307 that comprises A307D, A307G, A307P, A307S, or A307V;

at amino acid residue 308 that comprises K308I, K308Q, or K308R;

at amino acid residue 309 that comprises A309D or A309T;

at amino acid residue 310 that comprises L310I;

at amino acid residue 311 that comprises L311I;

at amino acid residue 312 that comprises Q312E, Q312K, or Q312L;

at amino acid residue 313 that comprises D313E or D313V;

at amino acid residue 314 that comprises K314E, K314M, K314N, or K314T;

at amino acid residue 315 that comprises D315A, D315G, D315H, D315N, D315V, or D315Y;

at amino acid residue 316 that comprises V316A or V316L;

at amino acid residue 317 that comprises I317L, I317M, or I317V;

at amino acid residue 318 that comprises A318D, A318P, A318T, or A318V;

at amino acid residue 319 that comprises I319M;

at amino acid residue 320 that comprises N320S or N320T;

at amino acid residue 321 that comprises Q321K;

at amino acid residue 322 that comprises D322A or D322V;

at amino acid residue 324 that comprises L324V or L324W; or

at amino acid residue 325 that comprises G325A, G325C, or G325V;

wherein the residues are numbered relative to SEQ ID NO:2.

26. The method of any of claims 1-25, wherein the at least one mutation includes a mutation:

at amino acid residue 326 that comprises K326E, K326M, K326Q, K326R, or K326T;

at amino acid residue 327 that comprises Q327H or Q327P;

at amino acid residue 329 that comprises Y329C, Y329D, Y329F, Y329H, or Y329N;

at amino acid residue 330 that comprises Q330E, Q330H, or Q330K;
at amino acid residue 331 that comprises L331H, L331P, L331R, or L331V;
at amino acid residue 332 that comprises R332G, R332I, R332S, or R332T;
at amino acid residue 333 that comprises Q333E, Q333L, Q333P, or G334R;
at amino acid residue 334 that comprises G334V;
at amino acid residue 335 that comprises D335A, D335E, D335G, D335V, or D335Y;
at amino acid residue 336 that comprises N336D, N336I, N336S, N336T, or N336Y;
at amino acid residue 337 that comprises F337C, F337L, F337V, or F337Y;
at amino acid residue 338 that comprises E338A, E338D, or E338G;
at amino acid residue 339 that comprises V339M;
at amino acid residue 341 that comprises E341A, E341Q;
at amino acid residue 343 that comprises P343A or P343S;
at amino acid residue 344 that comprises L344F, L344R, or L344V;
at amino acid residue 346 that comprises G346A, G346C, G346D, or G346V;
at amino acid residue 347 that comprises L347I;
at amino acid residue 348 that comprises A348D;
at amino acid residue 349 that comprises W349C or W349L; or
at amino acid residue 350 that comprises A350G, A350S, A350T, A350V;
wherein the residues are numbered relative to SEQ ID NO:2.

27. The method of any of claims 1-26, wherein the at least one mutation includes a mutation:
at amino acid residue 351 that comprises V351A or V351E;
at amino acid residue 352 that comprises A352S or A352T;
at amino acid residue 353 that comprises M353K, M353L, or M353T;
at amino acid residue 354 that comprises I354R;
at amino acid residue 355 that comprises N355D, N355H, N355S, or N355Y;
at amino acid residue 356 that comprises R356L;
at amino acid residue 357 that comprises Q357E;
at amino acid residue 359 that comprises I359F, I359L, I359N, I359S, or I359V;
at amino acid residue 362 that comprises P362A, P362H, P362R, or P362S;
at amino acid residue 363 that comprises R363G, R363L, or R363S;
at amino acid residue 364 that comprises S364C or S364P;

at amino acid residue 365 that comprises Y365D, Y365F, Y365N, or Y365S;
at amino acid residue 366 that comprises T366I, T366N, T366P, or T366S
at amino acid residue 367 that comprises I367F, I367L, or I367M;
at amino acid residue 368 that comprises A368G or A368P;
at amino acid residue 369 that comprises V369A, V369F, V369G, V369I, or V369L;
at amino acid residue 370 that comprises A370D, A370G, A370P, A370T, or A370V;
at amino acid residue 371 that comprises S371C or S371T;
at amino acid residue 373 that comprises G373A or G373C;
at amino acid residue 374 that comprises K374E, K374I, K374R, or K374T; or
at amino acid residue 375 that comprises G375R;
wherein the residues are numbered relative to SEQ ID NO:2.

28. The method of any of claims 1-27, wherein the at least one mutation includes a mutation:
at amino acid residue 376 that comprises V376E, V376G, V376L or V376M;
at amino acid residue 377 that comprises A377G, A377P, A377S, or A377T;
at amino acid residue 379 that comprises N379D, N379I, N379K, or N379T;
at amino acid residue 380 that comprises P380A, P380H, P380R, or P380T;
at amino acid residue 381 that comprises A381D;
at amino acid residue 383 that comprises F383C, F383I, or F383Y;
at amino acid residue 384 that comprises I384F, I384M, or I384T;
at amino acid residue 385 that comprises T385I;
at amino acid residue 386 that comprises Q386H, Q386K, or Q386L;
at amino acid residue 387 that comprises L387F, L387H, L387I, or L387R;
at amino acid residue 388 that comprises L388F, L388H, L388I, L388R, or L388V;
at amino acid residue 391 that comprises K391I, K391N, K391Q, or K391R;
at amino acid residue 392 that comprises R392G, R392K, R392M or R392W;
at amino acid residue 393 that comprises s K393E, K393N, K393Q, or K393T;
at amino acid residue 394 that comprises L394I, L394Q, or L394R;
at amino acid residue 395 that comprises G395R;
at amino acid residue 396 that comprises F396C, F396I, F396L, or F396V;
at amino acid residue 397 that comprises Y397C, Y397F, Y397H, Y397N, or Y397S;
or

at amino acid residue 398 that comprises E398G or E398Q;

at amino acid residue 394 that comprises W399G or W399R;

at amino acid residue 400 that comprises T400A, T400I, T400N, T400P, or T400S;

wherein the residues are numbered relative to SEQ ID NO:2.

29. The method of any of claims 1-28, wherein the at least one mutation includes a mutation:

at amino acid residue 401 that comprises S401A, S401L, or S401T;

at amino acid residue 402 that comprises R402G, R402M, R402S, R402T, or R402W;

at amino acid residue 403 that comprises L403F or L403V;

at amino acid residue 404 that comprises R404G, R404I, R404K, R404S, or R404T;

at amino acid residue 405 that comprises S405G;

at amino acid residue 406 that comprises H406D, H406L, or H406Q;

at amino acid residue 407 that comprises I407L, I407M, or I407T;

at amino acid residue 408 that comprises N408D, N408H or N408T;

at amino acid residue 409 that comprises P409L;

at amino acid residue 410 that comprises T410S;

at amino acid residue 411 that comprises G411A, G411C, or G411V;

at amino acid residue 412 that comprises T412A, T412I, or T412S;

at amino acid residue 413 that comprises V413F, V413G, or V413I;

at amino acid residue 414 that comprises L414F or L414V;

at amino acid residue 415 that comprises L415H or L415I;

at amino acid residue 416 that comprises Q416E, Q416H, or Q416L;

at amino acid residue 417 that comprises L417I;

at amino acid residue 418 that comprises E418A, E418D, E418K, or E418Q;

at amino acid residue 419 that comprises N419I, N419S, N419T, or N419Y;

at amino acid residue 420 that comprises T420K, T420P, T420R, or T420S;

at amino acid residue 421 that comprises M421I, M421K, M421L, M421R, or M421T;

at amino acid residue 422 that comprises Q422P;

at amino acid residue 423 that comprises M423I, M423K, M423L or M423T;

at amino acid residue 424 that comprises S424L;

at amino acid residue 425 that comprises L425F;

at amino acid residue 427 that comprises D427N; or

at amino acid residue 429 that comprises L429R;

wherein the residues are numbered relative to SEQ ID NO:2.

30. The method of any of the preceding claims, wherein administering migalastat or salt thereof that comprises administering migalastat or salt thereof to the subject every other day.

31. The method of any of the preceding claims, wherein administering migalastat or salt thereof that comprises administering to the subject a dose of about 100 to about 150 mg free base equivalent of the migalastat or salt thereof.

32. The method of any of the preceding claims, wherein administering migalastat or salt thereof that comprises administering to the subject a dose of about 123 mg free base equivalent of the migalastat or salt thereof.

33. The method of any of the preceding claims, wherein the migalastat or salt thereof enhances α-galactosidase A activity in the subject.

34. The method of any of the preceding claims, wherein the at least one mutation includes an HEK assay amenable mutation in α-galactosidase A

35. The method of any of the preceding claims, wherein the migalastat or salt thereof is administered orally.

36. The method of any of claims 1-34, wherein the migalastat or salt thereof is administered by injection.

37. A computer-implemented method comprising:

receiving an electronic communication that corresponds to an identification of a particular mutation;

querying a data store medium using the identification of the particular mutation, wherein the data store medium includes an identification of each of a set of amenable

mutations, and wherein each of the set of amenable mutations corresponds to a mutation listed in Table 2;

detecting a result of the query, wherein the result is indicative of whether the particular mutation is represented in the set of amenable mutations;

generating, based on the response, an output that is indicative of a suitability of treating a subject with the particular mutation with migalastat or a migalastat salt; and

transmitting the output.

38. The method of claim 37, wherein the electronic communication includes the identification of the particular mutation in a first format, and wherein the method further that comprises:

determining that the first format differs from a second format used by the data store;

extracting one or more components from the identification;

generating a second identification based on the components, the second identification being in the second format;

transmitting the second identification; and

receiving a second electronic communication that indicates that the second identification corresponds to the first identification, wherein the data store medium is queried in response to receiving the second electronic communication.

39. The method of claim 37 or 38, wherein the data store medium further includes an identification of a second set of amenable mutations, wherein each of the second set of amenable mutations corresponds to a mutation listed in Table 1, and wherein the result is further indicative of whether the particular mutation is represented in the second set of amenable mutations.

40. The method of any of claims 37-39, wherein the result includes a binary indication as to whether migalastat or migalastat salt is a suitable treatment for a condition attributed to the particular mutation.

41. The method of any of claims 37-40, further comprising:

transmitting webpage data to a user device, wherein the electronic communication is received from the user device, wherein the webpage data corresponds to a webpage, and

wherein the identification of the particular mutation corresponds to input detected at the webpage.

42. The method of any of claims 37-41, wherein the data store medium identifies at least 90% of the mutations listed in Table 2.

43. A system comprising:

one or more data processors; and

a non-transitory computer readable storage medium containing instructions which, when executed on the one or more data processors, cause the one or more data processors to perform actions including:

receiving an electronic communication that corresponds to an identification of a particular mutation;

querying a data store medium using the identification of the particular mutation, wherein the data store medium includes an identification of each of a set of amenable mutations, and wherein each of the set of amenable mutations corresponds to a mutation listed in Table 2;

detecting a result of the query, wherein the result is indicative of whether the particular mutation is represented in the set of amenable mutations;

generating, based on the response, an output that is indicative of a suitability of treating a subject with the particular mutation with migalastat or a migalastat salt; and

transmitting the output.

44. The system of claim 43, wherein the electronic communication includes the identification of the particular mutation in a first format, and wherein the actions further include:

determining that the first format differs from a second format used by the data store;

extracting one or more components from the identification;

generating a second identification based on the components, the second identification being in the second format;

transmitting the second identification; and

receiving a second electronic communication that indicates that the second identification corresponds to the first identification, wherein the data store medium is queried in response to receiving the second electronic communication.

45. The system of claim 43 or 44, wherein the data store medium further includes an identification of a second set of amenable mutations, wherein each of the second set of amenable mutations corresponds to a mutation listed in Table 1, and wherein the result is further indicative of whether the particular mutation is represented in the second set of amenable mutations.

46. The system of any of claims 43-45, wherein the result includes a binary indication as to whether migalastat or migalastat salt is a suitable treatment for a condition attributed to the particular mutation.

47. The system of any of claims 43-46, wherein the actions further include:

transmitting webpage data to a user device, wherein the electronic communication is received from the user device, and the identification of the particular mutation corresponds to input detected at the webpage.

48. The system of any of claims 43-47, wherein the data store medium identifies at least 90% of the mutations listed in Table 2.

49. A computer-program product tangibly embodied in a non-transitory machine-readable storage medium, including instructions configured to cause one or more data processors to perform actions including:

receiving an electronic communication that corresponds to an identification of a particular mutation;

querying a data store medium using the identification of the particular mutation, wherein the data store medium includes an identification of each of a set of amenable mutations, and wherein each of the set of amenable mutations corresponds to a mutation listed in Table 2;

detecting a result of the query, wherein the result is indicative of whether the particular mutation is represented in the set of amenable mutations;

generating, based on the response, an output that is indicative of a suitability of treating a subject with the particular mutation with migalastat or a migalastat salt; and

transmitting the output.

50. The computer-program product of claim 49, wherein the electronic communication includes the identification of the particular mutation in a first format, and wherein the actions further include:

determining that the first format differs from a second format used by the data store;

extracting one or more components from the identification;

generating a second identification based on the components, the second identification being in the second format;

transmitting the second identification; and

receiving a second electronic communication that indicates that the second identification corresponds to the first identification, wherein the data store medium is queried in response to receiving the second electronic communication.

51. The computer-program product of claim 49 or 50, wherein the data store medium further includes an identification of a second set of amenable mutations, wherein each of the second set of amenable mutations corresponds to a mutation listed in Table 1, and wherein the result is further indicative of whether the particular mutation is represented in the second set of amenable mutations.

52. The computer-program product of any of claims 49-51, wherein the result includes a binary indication as to whether migalastat or migalastat salt is a suitable treatment for a condition attributed to the particular mutation.

53. The computer-program product of any of claims 49-52, wherein the actions further include:

transmitting webpage data to a user device, wherein the electronic communication is received from the user device, and the identification of the particular mutation corresponds to input detected at the webpage.

54. The computer-program product of any of claims 49-53, wherein the data store medium identifies at least 90% of the mutations listed in Table 2.

55. A computer-implemented method comprising:

accessing a data store medium storing a data set unit storing a data set that identifies, for each mutation of a set of mutations, a degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the mutation is present, wherein the set of mutations includes one or more mutations listed in Table 2;

receiving a communication that identifies one or more particular mutations;

querying the data store medium using a representation of the one or more particular mutations;

detecting a result of the query that indicates, for each particular mutation of the one or more particular mutations, the degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the particular mutation is present;

determining a metric corresponding to a predicted efficacy of treating a subject having the one or more particular mutations with migalastat or a migalastat salt; and

outputting the metric.

56. The computer-implemented method of claim 55, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

57. The computer-implemented method of claim 55 or 56, wherein the metric is a binary indication as to whether a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

58. The computer-implemented method of any of claims 55-57, wherein the metric includes a number, category or descriptor indicating a predicted extent to which a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

59. The computer-implemented method of any of claims 55-58, wherein the result of the query indicates, for a particular mutation of the one or more particular mutations and as a result of the particular mutation not being detected within the data set, that the α-Gal A activity corresponding to the particular mutation is not responsive to migalastat or a migalastat salt.

60. The computer-implemented method of any of claims 55-59, wherein the set of mutations further includes one or more mutations listed in Table 1.

61. The computer-implemented method of any of claims 55-60, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

62. A system comprising:

one or more data processors; and

a non-transitory computer readable storage medium containing instructions which, when executed on the one or more data processors, cause the one or more data processors to perform actions including:

accessing a data set unit storing a data set that identifies, for each mutation of a set of mutations, a degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the mutation is present, wherein the set of mutations includes one or more mutations listed in Table 2;

receiving a communication that identifies one or more particular mutations;

querying the data set unit using a representation of the one or more particular mutations;

detecting a result of the query that indicates, for each particular mutation of the one or more particular mutations, the degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the particular mutation is present;

determining a metric corresponding to a predicted efficacy of treating a subject having the one or more particular mutations with migalastat or a migalastat salt; and

outputting the metric.

63. The system of claim 62, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

64. The system of claim 62 or 63, wherein the metric is a binary indication as to whether a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

65. The system of any of claims 62-64, wherein the metric includes a number, category or descriptor indicating a predicted extent to which a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

66. The system of any of claims 62-65, wherein the result of the query indicates, for a particular mutation of the one or more particular mutations and as a result of the particular mutation not being detected within the data set, that the α-Gal A activity corresponding to the particular mutation is not responsive to migalastat or a migalastat salt.

67. The system of any of claims 62-66, wherein the set of mutations further includes one or more mutations listed in Table 1.

68. The system of any of claims 62-67, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

69. A computer-program product tangibly embodied in a non-transitory machine-readable storage medium, including instructions configured to cause one or more data processors to perform actions including:

accessing a data set unit storing a data set that identifies, for each mutation of a set of mutations, a degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the mutation is present, wherein the set of mutations includes one or more mutations listed in Table 2;

receiving a communication that identifies one or more particular mutations;

querying the data set unit using a representation of the one or more particular mutations;

detecting a result of the query that indicates, for each particular mutation of the one or more particular mutations, the degree to which α-Gal A activity is responsive to migalastat or a migalastat salt when the particular mutation is present;

determining a metric corresponding to a predicted efficacy of treating a subject having the one or more particular mutations with migalastat or a migalastat salt; and

outputting the metric.

70. The computer-program product of claim 69, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

71. The computer-program product of claim 69 or 70, wherein the metric is a binary indication as to whether a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

72. The computer-program product of any of claims 69-71, wherein the metric includes a number, category or descriptor indicating a predicted extent to which a condition associated with the one or more particular mutations is amenable to treatment with migalastat or a migalastat salt.

73. The computer-program product of any of claims 69-72, wherein the result of the query indicates, for a particular mutation of the one or more particular mutations and as a result of the particular mutation not being detected within the data set, that the α-Gal A activity corresponding to the particular mutation is not responsive to migalastat or a migalastat salt.

74. The computer-program product of any of claims 69-73, wherein the set of mutations further includes one or more mutations listed in Table 1.

75. The computer-program product of any of claims 69-74, wherein the one or more particular mutations include a plurality of particular mutations, and wherein determining the metric includes identifying a minimum or maximum of the degrees to which α-Gal A activity is responsive to migalastat or a migalastat salt across the plurality of particular mutations.

76. A method of treating Fabry disease in a subject comprising:

accessing mutation information corresponding to the subject, the mutation information identifying one or more α-galactosidase A mutations;

determining, based on the mutation information, that the subject has a mutation for which α-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 μM migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α-Gal A corresponding to the mutation; and

in response to the determination, administering migalastat or a salt thereof to the subject.

77. The method of claim 76, wherein the α-Gal A activity is defined as the nmoles of free 4-MU released per milligram of protein per hour.

78. The method of claim 76 or 77, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 1% greater than the reference α-Gal A activity.

79. The method of claim 76 or 77, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 5% greater than the reference α-Gal A activity.

80. The method of claim 76 or 77, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 10% greater than the reference α-Gal A activity.

81. The method of claim 76 or 77, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 20% greater than the reference α-Gal A activity.

82. The method of any of claims 76-81, wherein the determination includes:

querying a data store medium with an identification of the one or more α-galactosidase A mutations;

receiving a result of the query.

83. The method of claim 82, wherein the result indicates that representation of the mutation is included in the data store.

84. The method of claim 82, wherein the result includes one or more values associated with a representation of the mutation in the data store, and wherein the method further includes comparing the one or more values or a processed version thereof to a predefined threshold.

85. A method comprising:

accessing mutation information corresponding to a subject, the mutation information identifying one or more α-galactosidase A mutations;

determining, based on the mutation information, that the subject has a mutation for which α-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 μM migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α-Gal A corresponding to the mutation; and

in response to the determination, outputting an indication that the mutation is amenable to treatment with migalastat or a salt thereof.

86. The method of claim 85, wherein the α-Gal A activity is defined as the nmoles of free 4-MU released per milligram of protein per hour.

87. The method of claim 85 or 86, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 1% greater than the reference α-Gal A activity.

88. The method of claim 85 or 86, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 5% greater than the reference α-Gal A activity.

89. The method of claim 85 or 86, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 10% greater than the reference α-Gal A activity.

90. The method of claim 85 or 86, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 20% greater than the reference α-Gal A activity.

91. The method of any of claims 85-90, wherein the determination includes:

querying a data store medium with an identification of the one or more α-galactosidase A mutations; and

receiving a result of the query.

92. The method of claim 91, wherein the result indicates that representation of the mutation is included in the data store.

93. The method of claim 91, wherein the result includes one or more values associated with a representation of the mutation in the data store, and wherein the method further includes comparing the one or more values or a processed version thereof to a predefined threshold.

94. The method of any of claims 85-93, further comprising:

receiving, from a user device, a first communication that includes the mutation information;

wherein outputting the indication includes, transmitting a second communication to the user device, the second communication including the indication.

95. A system comprising:

one or more data processors; and

a non-transitory computer readable storage medium containing instructions which, when executed on the one or more data processors, cause the one or more data processors to perform actions including:

accessing mutation information corresponding to a subject, the mutation information identifying one or more α-galactosidase A mutations;

determining, based on the mutation information, that the subject has a mutation for which α-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 μM migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α-Gal A corresponding to the mutation; and

in response to the determination, outputting an indication that the mutation is amenable to treatment with migalastat or a salt thereof.

96. The system of claim 95, wherein the α-Gal A activity is defined as the nmoles of free 4-MU released per milligram of protein per hour.

97. The system of claim 95 or 96, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 1% greater than the reference α-Gal A activity.

98. The system of claim 95 or 96, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 5% greater than the reference α-Gal A activity.

99. The system of claim 95 or 96, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 10% greater than the reference α-Gal A activity.

100. The system of claim 95 or 96, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 20% greater than the reference α-Gal A activity.

101. The system of any of claims 95-100, wherein the determination includes:

querying a data store medium with an identification of the one or more α-galactosidase A mutations; and

receiving a result of the query.

102. The system of claim 101, wherein the result indicates that representation of the mutation is included in the data store.

103. The system of claim 101, wherein the result includes one or more values associated with a representation of the mutation in the data store, and wherein the actions further include comparing the one or more values or a processed version thereof to a predefined threshold.

104. The system of any of claims 95-103, wherein the actions further include:

receiving, from a user device, a first communication that includes the mutation information;

wherein outputting the indication includes, transmitting a second communication to the user device, the second communication including the indication.

105. A computer-program product tangibly embodied in a non-transitory machine-readable storage medium, including instructions configured to cause one or more data processors to perform actions including:

accessing mutation information corresponding to a subject, the mutation information identifying one or more α-galactosidase A mutations;

determining, based on the mutation information, that the subject has a mutation for which α-Gal A activity in lysates prepared from HEK-293 cells transiently transfected with a mutant form of α-Gal A and incubated for 5 days in the presence of 10 μM migalastat is greater than a reference α-Gal A activity in other lysates prepared from other HEK-293 cells transiently transfected with the mutant form of α-Gal A and incubated for 5 days in the absence of 10 μM migalastat, the mutant form of α-Gal A corresponding to the mutation; and

in response to the determination, outputting an indication that the mutation is amenable to treatment with migalastat or a salt thereof.

106. The computer-program product of claim 105, wherein the α-Gal A activity is defined as the nmoles of free 4-MU released per milligram of protein per hour.

107. The computer-program product of claim 105 or 106, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 1% greater than the reference α-Gal A activity.

108. The computer-program product of claim 105 or 106, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 5% greater than the reference α-Gal A activity.

109. The computer-program product of claim 105 or 106, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 10% greater than the reference α-Gal A activity.

110. The computer-program product of claim 105 or 106, wherein the determination includes determining that the subject has a mutation for which α-Gal A activity is at least 20% greater than the reference α-Gal A activity.

111. The computer-program product of any of claims 105-110, wherein the determination includes:

querying a data store medium with an identification of the one or more α-galactosidase A mutations; and

receiving a result of the query.

112. The computer-program product of claim 111, wherein the result indicates that representation of the mutation is included in the data store.

113. The computer-program product of claim 111, wherein the result includes one or more values associated with a representation of the mutation in the data store, and wherein the actions further include comparing the one or more values or a processed version thereof to a predefined threshold.

114. The computer-program product of any of claims 105-113, wherein the actions further include:

receiving, from a user device, a first communication that includes the mutation information;

wherein outputting the indication includes, transmitting a second communication to the user device, the second communication including the indication.

115. A method for treatment of Fabry disease in a human patient in need thereof, the method comprising administering to the patient a therapeutically effective dose of migalastat or a salt thereof, wherein the patient has an α-galactosidase A mutation selected from the group consisting of those mutations provided in Table 2.

116. A method of enhancing α-galactosidase A in a patient diagnosed with or suspected of having Fabry disease, the method comprising administering to the patient a therapeutically effective dose of migalastat or a salt thereof, wherein the patient has an α-galactosidase A mutation selected from the group consisting of those mutations provided in Table 2.

117. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, and L10Q.

118. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, and R17P.

119. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, and G28R.

120. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, and R38W.

121. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V and N53H.

122. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, and P60R.

123. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, and L68I.

124. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, and L75F.

125. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, and K82R.

126. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, and I91F.

127. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, and D101V.

128. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, and D109A.

129. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, and H125D.

130. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, and D136N.

131. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I,

N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, and G144A.

132. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, and Y151D.

133. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, and F159V.

134. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, and F169L.

135. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, and E178A.

136. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, and H186D.

137. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, and L191V.

138. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, and S197I.

139. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, and L206V.

140. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, and N215H.

141. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, and I219M.

142. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, and F229Y.

143. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, and K240M.

144. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, and T246R.

145. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, and E251V.

146. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G, D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, and P259A.

147. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, and L275I.

148. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, and L286V.

149. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, and N298T.

150. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, and K308Q.

151. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, and D315Y.

152. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, and G325V.

153. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E, Q330H, Q330K, L331H, L331P, L331R, L331V, and R332G.

154. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, and F337L.

155. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: F337V, F337Y, E338A, E338D, E338G, V339M, E341A, E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, and W349C.

156. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, and I359F.

157. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, and T366P.

158. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, and G373C.

159. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, and P380R.

160. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, and L388R.

161. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N, K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, and F396L.

162. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, and R402M.

163. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, and N408T.

164. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, and E418A.

165. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P,

T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, and M423L.

166. The method of claim 115 or 116, wherein the mutation is selected from the group consisting of: M423T, S424L, L425F, D427N, and L429R.

167. The method of any one of claims 115-166, wherein the migalastat or salt thereof is administered to the patient every other day.

168. The method of any one of claims 115-167, wherein the patient is administered about 100 to about 150 mg free base equivalent of the migalastat or salt thereof every other day.

169. The method of any one of claims 115-168, wherein the patient is administered about 123 mg free base equivalent of the migalastat or the salt thereof every other day.

170. The method of any one of claims 115-169, wherein the patient is administered about 123 mg of migalastat free base every other day.

171. The method of one of claims 115-169, wherein the patient is administered about 150 mg of migalastat hydrochloride every other day.

172. The method of any one of claims 115-171, wherein the migalastat or salt thereof enhances α-galactosidase A activity.

173. The method of one of claims 115-172, wherein the mutation is disclosed in a pharmacological reference table.

174. The method of claim 173, wherein the pharmacological reference table is provided in a product label for a migalastat product approved for the treatment of Fabry disease.

175. The method of claim 173, wherein the pharmacological reference table is provided in a product label for GALAFOLD®.

176. The method of claim 173, wherein the pharmacological reference table is provided at a website.

177. The method of claim 176, wherein the website is one or more of www.galafoldamenabilitytable.com or www.fabrygenevariantsearch.com.

178. The method of any one of claims 115-177, wherein the migalastat or salt thereof is administered orally.

179. The method of any one of claims 115-177, wherein the migalastat or salt thereof is administered by injection.

180. The method of any one of claims 115-179, wherein the patient is male.

181. The method of any one of claims 115-179, wherein the patient is female.

182. A method for treatment of Fabry disease in a human patient in need thereof, the method comprising administering to the patient a therapeutically effective dose of migalastat or a salt thereof, wherein the patient has a HEK assay amenable mutation in α-galactosidase A disclosed in a pharmacological reference table, wherein the pharmacological reference table includes one or more mutations from Table 2.

183. A method of enhancing α-galactosidase A in a patient diagnosed with or suspected of having Fabry disease, the method comprising administering to the patient a therapeutically effective dose of migalastat or a salt thereof, wherein the patient has a HEK assay amenable mutation in α-galactosidase A disclosed in a pharmacological reference table, wherein the pharmacological reference table includes one or more mutations from Table 2.

184. The method of claim 182 or 183, wherein the pharmacological reference table includes all of the mutations from Table 2.

185. The method of any one of claims 182-184, wherein the pharmacological reference table includes one or more mutations from Table 1.

186. The method of any one of claims 182-185, wherein the pharmacological reference table includes all of the mutations from Table 1.

187. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: N5D, N5K, P6L, P6Q, P6R, P6S, P6T, E7D, E7K, E7V, L8I, L8P, L8Q, H9L, H9Q, H9R, H9Y, L10M, L10P, and L10Q.

188. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: L10R, L10V, G11C, G11D, G11R, G11S, G11V, C12G, C12R, C12S, C12Y, A13E, A13G, L14F, L14H, L14V, R17C, R17G, R17H, and R17P.

189. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: R17S, F18I, F18L, A20G, L21H, V22A, V22F, V22I, V22L, S23P, S23T, W24S, D25H, I26N, P27A, P27L, P27S, P27T, G28E, and G28R.

190. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: G28W, A29G, A29P, A29V, R30G, L32M, L32Q, L32R, L32V, D33A, D33E, D33V, L36M, L36V, A37E, A37G, A37S, R38G, R38M, and R38W.

191. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: T39A, T39K, T39M, T39R, T39S, T41A, T41N, T41S, G43A, L45M, L45V, H46D, H46N, H46Q, E48A, F50Y, M51R, M51T, M51V and N53H.

192. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: N53I, N53S, N53T, L54H, L54R, L54V, D55A, D55E, D55H, D55Y, C56W, E58K, E59A, E59D, E59G, E59Q, E59V, P60A, P60Q, and P60R.

193. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: D61E, D61V, S62A, S62C, S62F, S62P, S62Y, I64L, I64V, S65C, S65G, S65R, E66D, E66V, K67E, K67M, K67N, K67Q, K67T, and L68I.

194. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: F69I, F69Y, M70I, M70K, M70L, M70R, E71A, E71D, E71G, E71Q, E71V, M72L, M72T, A73S, A73T, E74D, E74G, E74K, E74V, and L75F.

195. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: L75P, M76V, V77I, V77L, S78L, S78P, E79A, E79D, E79G, E79K, E79Q, E79V, G80A, G80C, G80S, W81L, K82E, K82M, K82N, and K82R.

196. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: K82T, D83A, D83E, D83G, D83V, A84E, A84G, A84P, A84S, A84T, A84V, G85A, G85C, G85R, Y86F, E87G, Y88H, Y88N, L89V, and I91F.

197. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: I91L, I91M, I91S, M96L, M96T, A97D, A97S, A97T, P98H, P98L, P98R, Q99E, Q99L, Q99P, Q99R, D101A, D101E, D101G, D101H, and D101V.

198. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: S102A, S102P, S102T, G104A, G104D, G104S, R105G, R105I, R105K, R105T, L106H, L106I, L106P, L106V, Q107E, Q107H, Q107K, A108E, A108V, and D109A.

199. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: D109E, D109H, D109N, D109Y, P110T, F113V, F113Y, P114L, H115D, H115N, G116R, I117M, I117T, A121V, Y123D, Y123F, Y123N, Y123S, V124I, and H125D.

200. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: H125N, H125R, S126C, S126I, K127E, G128A, L129V, K130M, K130N, K130Q, L131V, I133L, I133T, I133V, A135E, A135G, A135S, A135T, D136A, and D136N.

201. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: D136V, V137A, V137D, V137G, V137I, V137L, G138A, N139H, N139I, N139K, N139Y, K140E, K140I, K140N, K140Q, K140R, T141S, A143E, A143G, and G144A.

202. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: G144C, G144R, G144S, F145C, F145L, F145V, F145Y, P146A, P146H, P146L, P146T, G147A, S148C, S148G, S148T, F149C, G150E, G150V, Y151C, and Y151D.

203. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: Y151S, Y152F, Y152S, D153A, D153H, D153N, D153V, D153Y, A156G, Q157E, Q157K, Q157L, Q157P, T158A, T158I, T158N, T158S, F159I, F159L, and F159V.

204. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: F159Y, A160G, A160S, A160T, A160V, D161H, D161N, D161V, D161Y, W162S, V164A, V164I, V164L, D165A, D165E, L166M, L166Q, L167I, F169C, and F169L.

205. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: F169V, F169Y, G171A, G171V, Y173C, Y173F, Y173H, Y173S, D175G, D175H, D175V, D175Y, S176C, S176R, L177F, L177M, L177S, L177V, L177W, and E178A.

206. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: E178G, E178K, E178Q, L180M, L180S, A181P, A181T, A181V, D182A, D182E, D182V, D182Y, Y184F, Y184H, Y184S, K185M, K185N, K185Q, K185T, and H186D.

207. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: H186L, H186N, H186Q, H186Y, M187L, S188A, S188C, S188F, S188P, S188T, S188Y, L189S, L189V, A190D, A190G, A190S, A190T, A190V, L191M, and L191V.

208. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: N192D, N192H, N192K, N192S, N192T, R193G, R193M, R193T, R193W, T194N, T194P, T194S, G195C, G195R, G195S, R196I, R196K, S197C, S197G, and S197I.

209. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: S197N, S197T, I198M, I198S, V199E, V199L, Y200N, Y200S, S201A, S201C, S201T, E203A, E203G, E203Q, W204S, L206F, L206H, L206I, L206R, and L206V.

210. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: Y207F, M208K, W209C, W209G, P210H, P210T, F211C, F211L, F211S, F211V, F211Y, Q212H, Q212P, K213E, K213Q, P214A, P214H, P214R, P214T, and N215H.

211. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: N215K, N215T, N215Y, Y216F, Y216H, Y216N, T217A, T217I, T217K, T217P, T217R, T217S, E218A, E218D, E218G, E218K, E218Q, E218V, I219F, and I219M.

212. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: I219S, R220L, Q221E, Q221H, Q221K, Q221L, Q221R, Y222C, Y222D, Y222H, Y222N, Y222S, N224H, R227G, N228H, N228I, N228T, F229I, F229S, and F229Y.

213. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: A230D, A230G, A230P, A230V, I232L, I232M, I232V, D233A, D233E, D233G, D233V, S235A, S235T, K237I, S238C, S238I, S238T, I239L, K240E, and K240M.

214. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: K240R, S241C, S241I, S241T, I242L, I242M, I242S, L243M, L243S, L243V, D244A, D244E, D244G, D244V, D244Y, W245C, T246A, T246I, T246K, and T246R.

215. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: S247A, S247F, S247T, S247Y, F248C, F248L, F248V, F248Y, N249D, N249H, N249I, N249S, N249T, N249Y, Q250E, Q250L, E251G, E251K, E251Q, and E251V.

216. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: R252G, I253F, I253N, I253V, V254A, V254D, V254F, V254G,

D255A, D255E, D255H, D255N, D255V, D255Y, V256D, V256G, V256L, A257S, G258E, and P259A.

217. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: P259T, G260W, G261A, N263H, N263T, D264H, D264N, P265A, P265Q, M267L, M267V, L268F, L268I, V269L, I270L, I270S, I270V, N272D, F273Y, and L275I.

218. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: W277L, N278I, Q280L, Q280R, V281A, V281E, V281G, V281L, T282S, Q283E, Q283H, Q283L, M284I, M284L, A285G, A285T, A285V, L286F, L286H, and L286V.

219. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: A288G, A288S, A288V, I289L, I289T, I289V, A291G, A292G, A292S, L294F, L294I, L294V, F295I, F295S, F295V, F295Y, S297T, N298D, N298I, and N298T.

220. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: D299H, D299N, L300I, L300V, H302D, H302L, H302N, H302Y, I303S, S304I, Q306E, Q306L, Q306P, A307D, A307G, A307P, A307S, A307V, K308I, and K308Q.

221. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: K308R, A309D, A309T, L310I, L311I, Q312E, Q312K, Q312L, D313E, D313V, K314E, K314M, K314N, K314T, D315A, D315G, D315H, D315N, D315V, and D315Y.

222. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: V316A, V316L, I317L, I317M, I317V, A318D, A318P, A318T, A318V, I319M, N320S, N320T, Q321K, D322A, D322V, L324V, L324W, G325A, G325C, and G325V.

223. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: K326E, K326M, K326Q, K326R, K326T, Q327H, Q327P, Y329C, Y329D, Y329F, Y329H, Y329N, Q330E, Q330H, Q330K, L331H, L331P, L331R, L331V, and R332G.

224. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: R332I, R332S, R332T, Q333E, Q333L, Q333P, G334R, G334V, D335A, D335E, D335G, D335V, D335Y, N336D, N336I, N336S, N336T, N336Y, F337C, and F337L.

225. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: F337V, F337Y, E338A, E338D, E338G, V339M, E341A, E341Q, P343A, P343S, L344F, L344R, L344V, G346A, G346C, G346D, G346V, L347I, A348D, and W349C.

226. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: W349L, A350G, A350S, A350T, A350V, V351A, V351E, A352S, A352T, M353K, M353L, M353T, I354R, N355D, N355H, N355S, N355Y, R356L, Q357E, and I359F.

227. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: I359L, I359N, I359S, I359V, P362A, P362H, P362R, P362S, R363G, R363L, R363S, S364C, S364P, Y365D, Y365F, Y365N, Y365S, T366I, T366N, and T366P.

228. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: T366S, I367F, I367L, I367M, A368G, A368P, V369A, V369F, V369G, V369I, V369L, A370D, A370G, A370P, A370T, A370V, S371C, S371T, G373A, and G373C.

229. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: K374E, K374I, K374R, K374T, G375R, V376E, V376G, V376L, V376M, A377G, A377P, A377S, A377T, N379D, N379I, N379K, N379T, P380A, P380H, and P380R.

230. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: P380T, A381D, F383C, F383I, F383Y, I384F, I384M, I384T, T385I, Q386H, Q386K, Q386L, L387F, L387H, L387I, L387R, L388F, L388H, L388I, and L388R.

231. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: L388V, K391I, K391N, K391Q, K391R, R392G, R392K, R392M, R392W, K393E, K393N, K393Q, K393T, L394I, L394Q, L394R, G395R, F396C, F396I, and F396L.

232. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: F396V, Y397C, Y397F, Y397H, Y397N, Y397S, E398G, E398Q, W399G, W399R, T400A, T400I, T400N, T400P, T400S, S401A, S401L, S401T, R402G, and R402M.

233. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: R402S, R402T, R402W, L403F, L403V, R404G, R404I, R404K, R404S, R404T, S405G, H406D, H406L, H406Q, I407L, I407M, I407T, N408D, N408H, and N408T.

234. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: P409L, T410S, G411A, G411C, G411V, T412A, T412I, T412S, V413F, V413G, V413I, L414F, L414V, L415H, L415I, Q416E, Q416H, Q416L, L417I, and E418A.

235. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: E418D, E418K, E418Q, N419I, N419S, N419T, N419Y, T420K, T420P, T420R, T420S, M421I, M421K, M421L, M421R, M421T, Q422P, M423I, M423K, and M423L.

236. The method of any one of claims 182-186, wherein the mutation is selected from the group consisting of: M423T, S424L, L425F, D427N, and L429R.

237. The method of any one of claims 182-236, wherein the migalastat or salt thereof is administered to the patient every other day.

238. The method of any one of claims 182-237, wherein the patient is administered about 100 to about 150 mg free base equivalent of the migalastat or salt thereof every other day.

239. The method of any one of claims 182-238, wherein the patient is administered about 123 mg free base equivalent of the migalastat or the salt thereof every other day.

240. The method of any one of claims 182-239, wherein the patient is administered about 123 mg of migalastat free base every other day.

241. The method of any one of claims 182-239, wherein the patient is administered about 150 mg of migalastat hydrochloride every other day.

242. The method of any one of claims 182-241, wherein the migalastat or salt thereof enhances α-galactosidase A activity.

243. The method of any one of claims 182-242, wherein the pharmacological reference table is provided in a product label for a migalastat product approved for the treatment of Fabry disease.

244. The method of any one of claims 182-243, wherein the pharmacological reference table is provided in a product label for GALAFOLD®.

245. The method of any one of claims 182-243, wherein the pharmacological reference table is provided at a website.

246. The method of claim 182-245, wherein the website is one or more of www.galafoldamenabilitytable.com or www.fabrygenevariantsearch.com.

247. The method of any one of claims 182-246, wherein the migalastat or salt thereof is administered orally.

248. The method of any one of claims 182-246, wherein the migalastat or salt thereof is administered by injection.

249. The method of any one of claims 182-248, wherein the patient is male.

250. The method of any one of claims 182-248, wherein the patient is female.