The Validation of Pharmacogenetics for the Identification of Fabry Patients for Treatment with Migalastat

Supplementary Information

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Benjamin et al., 2016

TABLE OF CONTENTS.

Transient Transfection and Migalastat Incubation

HEK-293 cells were plated in 96-well plates at 7500 cells in 100 µL cell culture media per well and incubated overnight at 37°C with 5% CO_2. To transfect the cells, plasmid DNA was incubated with the FuGENE lipid-based transfection reagent as previously described [1], and then 5 µL of transfection reaction [1] was added to each well of cells in the 96-well plate. Each plate contained three controls: WT-*GLA* in Column 1, pcDNA vector control in Column 2, and R301Q, a mutant that is known to be responsive to migalastat, in Column 12. Up to nine different α-Gal A mutant-expressing plasmids were added to Columns 3-11 of the plate, with a different plasmid in each column. One hour following transfection, migalastat was diluted to 200 µM in cell culture media and then 5.5 µL of 200 µM AT1001 was added to rows E-H of the 96-well plate for a final concentration of 10 µM migalastat in a final volume of 110.5 µL. 5.5 µL of cell culture media alone was added to rows A-D of the plate. Cells were then incubated for five days at 37°C with 5% CO_2. To prevent evaporation over the extended incubation time, all incubations were performed at greater than 95% relative humidity in a humidity chamber. The concentration of 10 µM migalastat is used in this assay because it is the approximate maximum concentration of migalastat in the plasma of patients with Fabry disease following a single oral dose of 150 mg [2].

α-Gal A Enzyme Activity Measurement

After five days, excess migalastat was removed by washing cells twice with phosphate-buffered saline (PBS) and then incubating in migalastat-free cell culture media for two hours at 37°C with 5% CO_2. Cells were washed again twice with PBS and then lysed by adding lysis buffer (27 mM sodium citrate, 46 mM sodium phosphate dibasic, 0.5% Triton X-100, pH 4.6). A volume of 65 µL of lysis buffer was added per well, and plates were incubated on a plate shaker at 150 rpm for 30 minutes at room temperature.

After the 30-minute lysis, cell lysate containing solubilized α-Gal A was transferred to a new 96-well plate. α-Gal A activity was measured in 10 µL cell lysate, both undiluted and diluted 1:30 in 0.1 µg/µL untransfected HEK-293 cell lysate, by incubation with 4-methylumbelliferone-α-D-galactopyranoside and *N*-acetyl-D-galactosamine as previously described [1] for one hour at 37°C. Stop buffer was then added to the reaction and fluorescence was read using 355 nm excitation and 460 nm emission wavelengths on a SpectraMax Plus 5e spectrophotometer (Molecular Devices Corp., Sunnyvale, CA). The amount of 4-MU generated in the assay was calculated based on a 4-methylumbelliferone (4-MU) standard curve (ranging from 29 nM to 30 µM) run on a separate plate. If results from either the undiluted or the 1:30-diluted cell lysate were above the lower limit of quantification (29 nM) but neither result was within the range of the 4-MU standard curve, then the enzyme assay was repeated within three hours of lysis using a higher dilution.

To normalize for the total cellular protein, a protein assay (Pierce Bicinchoninic Acid Protein Assay, Thermo Fisher Scientific Inc.) was performed according to the manufacturer's instructions on 25 µL of cell lysate from each well.

α-Gal A activity from every well was expressed as nmoles of 4-MU/mg protein/hour. The endogenous HEK-293 cellular α-Gal A activity was measured in lysates from pcDNA-transfected wells that were incubated either in the absence or presence of 10 µM migalastat. The final α-Gal A activity in each well of transfected mutant *GLA*, WT-*GLA*, and R301Q was calculated after subtracting the average activity of pcDNA-transfected wells that were incubated either in the absence or presence of 10 µM migalastat in parallel from the same plate.

Quantitative Polymerase Chain Reaction Test

After the 30-minute lysis (described above), the layer of cells that remained on the bottom of each well in the cell culture plate was analyzed by quantitative polymerase chain reaction (qPCR) for the presence of plasmid DNA as a transfection control. To access plasmid DNA within the layer of cells that remained on the bottom of the cell culture plate, cells were further lysed using an SDS-based lysis buffer in a final volume of 65 µL, and then the lysate was diluted 1:30 in nuclease-free water and used directly in the qPCR reaction. qPCR was performed on a 384-well plate, with lysate from up to three different 96-well plates in three quadrants and standards and quality controls in the fourth quadrant.

The qPCR reaction utilized a FAM-labeled Taqman probe with an MGB non-fluorescent quencher, with primers that amplified a 73-basepair region of the plasmid that spanned the junction between the 3' end of the *GLA* cDNA and the pcDNA vector. The qPCR reaction was run on a ViiA-7 Real-Time PCR System using "fast" chemistry, with 40 cycles consisting of 95°C for one second and 60°C for 20 seconds per cycle. Data were collected at the end of each cycle.

Cycle threshold values for each well were compared to a standard curve of WT-*GLA* plasmid DNA diluted in nuclease-free water to calculate the final reported value of pg DNA per well. Assay acceptance criteria: 1) reportable pg DNA per well values were required to be between 6.25 and 480 pg DNA per well (the lower and upper limits of quantification, respectively), 2) pg DNA values per well in each column of the transfection plate containing pcDNA with the *GLA* insert (regardless of treatment group, n=8) were required to have a %CV≤10, 3) the result for the pcDNA-transfected control was required to be below the lower limit of quantification (6.25 pg DNA per well), 4) for each plasmid tested in a transfection plate (each column, n=8), the average pg DNA per well value was required to be at least 40% of the average pg DNA per well value of WT-*GLA* in Column 1 of the same transfection plate. For example, if the average value for WT-*GLA* was measured as 100 pg DNA per well, the average value of R301Q must be ≥40 pg DNA per well. The final GLP HEK assay result for transfected *GLA* mutants without a sufficient quantity of *GLA* cDNA recovered was pre-specified to be "no conclusion."

Determination of the Mutant α-Gal A Response to Migalastat

Twenty separate determinations of α-Gal A activity from five different assays with n=4 per assay for each condition (with or without migalastat) for each mutant form were obtained. The results were then used to calculate the average ± SEM α-Gal A activity in nmol/mg/hour for the twenty data points for each treatment. If this value was below the limit of detection (142 nmol/mg/hour), then the average value was reported as below the limit of detection.

The % wild-type activity value for each mutant α-Gal A was calculated based on the average (n=4) baseline wild-type value on the same plate on the same day (plate acceptance criteria for the average baseline wild-type α-Gal A activity was 18000 to 60000 nmol/mg/hour with a precision (CV%) ≤30%). The average ± SEM of the mutant α-Gal A % wild-type values for the twenty data points for each condition was then calculated. To calculate the absolute increase, the average mutant α-Gal A % wild-type baseline value was subtracted from the average mutant α-Gal A % wild-type from migalastat-incubated wells. The α-Gal A activity –fold over baseline was calculated by dividing the average nmol/mg/hour value from migalastat-incubated wells by the average nmol/mg/hour baseline value.

Differences in α-Gal A activity measured in migalastat-incubated versus baseline were determined using a one-tailed Mann-Whitney U non-parametric test (GraphPad Prism, version 4.02). The difference was considered significant if incubation with migalastat resulted in an increase in activity with $p<0.05$.

Statistical Analyses

The degree of consistency between pairs of datasets was evaluated by calculating the sensitivity, specificity, positive predictive value, negative predictive value, and each of the 95% confidence intervals, using Microsoft Office Excel 2007 (Redmond, WA) and the Center for Clinical Research and Biostatistics website.

Analyses to determine *p*-values for statistically significant increases in mutant α-Gal A activity of transfected HEK-293 cells incubated with and without migalastat by one-tailed Mann Whitney-U test were carried out using GraphPad Prism, version 4.02 (San Diego, CA). Absolute change from baseline in Fabry substrate (i.e., kidney interstitial capillary GL-3 or plasma lyso-Gb_3) is calculated as the value after 6 months of migalastat treatment minus the value prior to treatment. The mean baseline (minimum, maximum), mean changes from baseline (95% confidence interval), and mean difference (95% confidence interval) in the change from baseline after 6 months were calculated using SAS, version 9.4 (Cary, NC). The GLP HEK assay α-Gal A activity –fold over baseline and absolute increase at 10 μM migalastat were calculated using Microsoft Office Excel 2007 according to Equations 1 and 2 (see below). The α-Gal A activity –fold over baseline and absolute increase at 10 μM migalastat mean, standard error of the mean, and 95% confidence intervals were calculated using GraphPad prism, version 4.02.

Equation 1:

$$\alpha - \text{Gal A activity} - \text{fold over baseline} = \frac{\alpha\text{–Gal A activity at 10 } \mu\text{M migalastat}}{\text{Baseline } \alpha\text{–Gal A activity}}$$

Equation 2:

$$\text{Absolute Increase (\% WT)} = (\text{\% WT } \alpha\text{-Gal A activity at 10 } \mu\text{M migalastat}) - (\text{\% WT at baseline})$$

RESULTS

Sensitivity and Specificity Calculations for Mutant α-Gal A Responses to Migalastat in the GLP HEK Assay and 74 Male Fabry Patient-Derived Lymphoblast Cell Lines

27/74 mutant forms met the amenability criteria in male Fabry patient-derived lymphoblasts. 25/ 27 mutant forms met the amenability criteria in the GLP HEK assay. Therefore, the sensitivity was calculated to be 0.92 (25 ÷ 27). Forty-seven of the 74 mutant forms did not meet the amenability criteria in male Fabry patient-derived lymphoblasts; Forty-two of these 47 mutant forms did not meet the criteria in the GLP HEK assay. Therefore, the specificity was calculated to be 0.89 (42 ÷ 47).

Comparison of Mutant α-Gal A Responses to Migalastat in the GLP HEK Assay and PBMCs in 51 Male Fabry Patients from Phase 2 and 3 Clinical Studies

Calculations for all male patients receiving 150 mg migalastat HCl QOD are provided below (Data are provided in Tables 3S-6S):

1. Sensitivity: Thirty-five male patients showed positive PBMC α-Gal A responses to migalastat (defined as an increase in α-Gal A levels of at least 2.0% of normal in PBMCs). The mutant forms of 35 of those patients consistently had responses to 10 μM migalastat in the GLP HEK assay that met the amenable mutation criteria. The sensitivity was calculated to be 1.0 (35 ÷ 35); 95% confidence intervals, 1.0, 1.0.
2. Specificity: Sixteen male patients showed less than 2.0% of normal increases in α-Gal A levels in PBMCs in response to migalastat. Fourteen of the 16 patients did not meet the amenable mutation criteria in the GLP HEK assay. The specificity was calculated to be 0.875 (14 ÷ 16); 95% confidence intervals, 0.7130, 1.0371.
3. Positive predictive value: Amenable mutant forms were represented in 37 male patients. Thirty-five of the 37 patients showed positive PBMC α-Gal A responses to oral administration of migalastat. The positive predictive value was calculated to be 0.9460 (35 ÷ 37); 95% confidence intervals, 0.8731, 1.0188.
4. Negative predictive value: Non-amenable mutant forms were represented in 14 male patients. All 14 patients showed less than 2.0% of normal increases in α-Gal A levels in PBMCs in response to migalastat. The negative predictive value was calculated to be 1.0 (14 ÷ 14); 95% confidence intervals (1.0, 1.0).

Comparison of Mutant α-Gal A Responses to Migalastat in the GLP HEK Assay and Fabry Patient Substrate Responses

Kidney Interstitial Capillary GL-3

Predictive calculations for male patients in Study 011 (Data are provided in Table 7S):

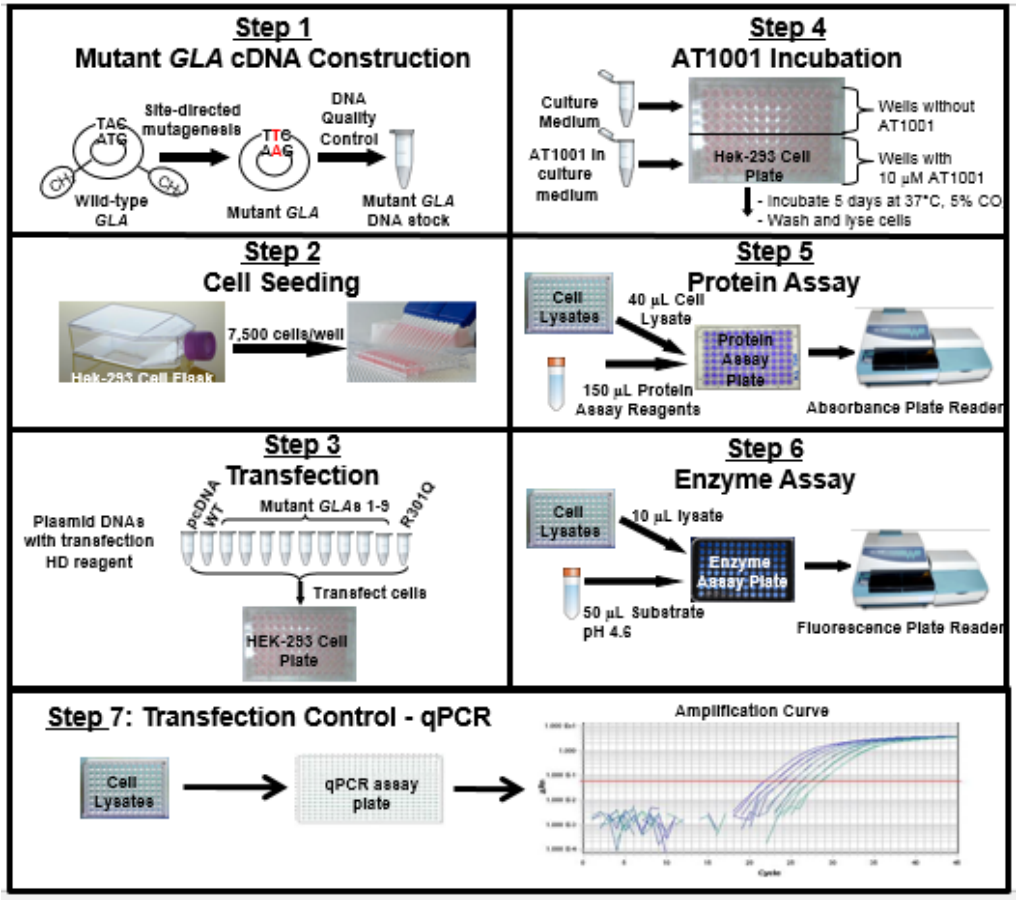
1. Sensitivity: Twelve of 12 male patients that met the amenable mutation criteria in the GLP HEK assay showed positive responses. The sensitivity was calculated to be 1.0 (12 ÷ 12); 95% confidence intervals, 1.0, 1.0.
2. Specificity: Six male patients did not have a positive response in disease substrate. None of the 6 patients met the amenable mutation criteria in the GLP HEK assay. The specificity was calculated to be 1.0 (6 ÷ 6); 95% confidence intervals, 1.0, 1.0.
3. Positive Predictive Value: Amenable mutant forms were represented in 12 male patients. All 12 patients showed a positive kidney interstitial capillary GL-3 response. The positive predictive value was calculated to be 1.0 (12 ÷ 12); 95% confidence intervals, 1.0, 1.0.
4. Negative Predictive Value: Non-amenable mutant forms were represented in 6 male patients. None of the 6 patients showed a positive response in kidney interstitial capillary GL-3. The negative predictive value in these patients was calculated to be 1.0 (6 ÷ 6 = 1.0); 95% confidence intervals, 1.0, 1.0.

Plasma Lyso-Gb_3

Predictive calculations for male patients in Study 011 (Data are provided in Table 8S):

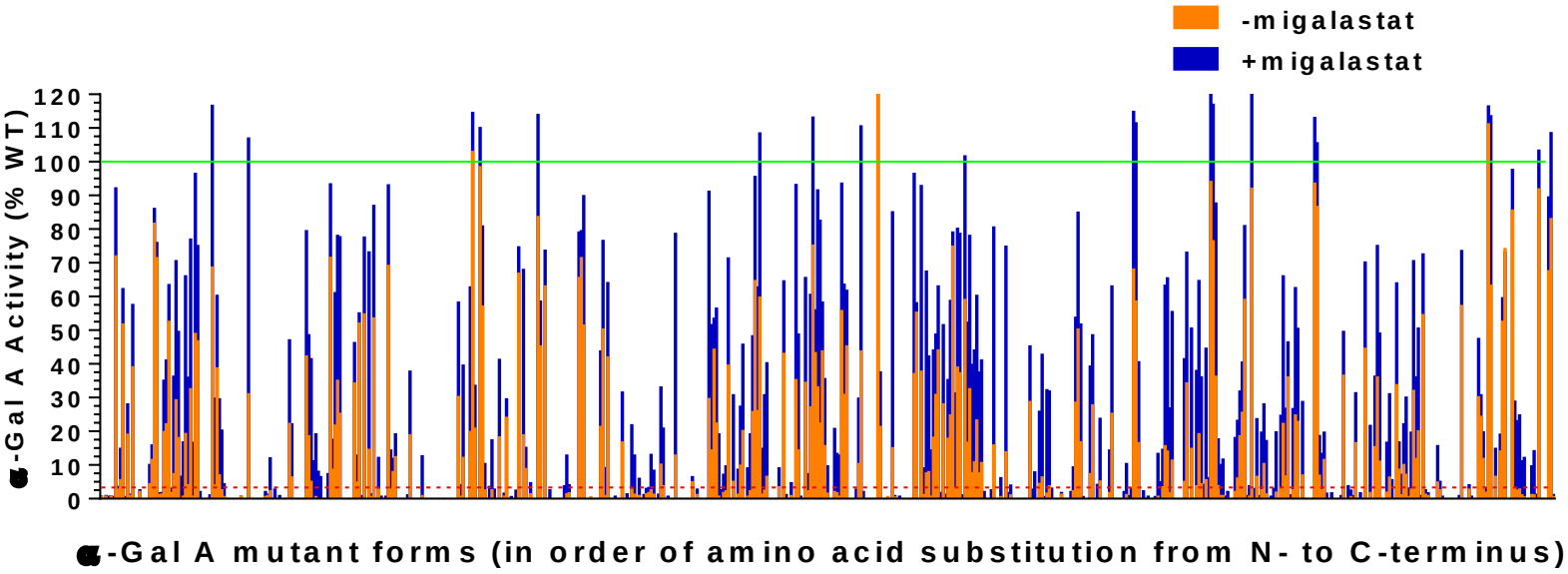
1. Sensitivity: Eleven of 11 male patients with mutant α-Gal A responses that met the amenable mutation criteria in the GLP HEK assay showed a positive lyso-Gb_3 response. The sensitivity was calculated to be 1.0 (11 ÷ 11); 95% confidence intervals, 1.0, 1.0.
2. Specificity: Five male patients did not show a positive plasma lyso-Gb_3 response. None of the 5 met the amenable mutation criteria in the GLP HEK assay. The specificity was calculated to be 1.0 (5 ÷ 5); 95% confidence intervals, 1.0, 1.0.
3. Positive Predictive Value: Amenable mutant forms were represented in 11 male patients. All 11 patients showed positive plasma lyso-Gb_3 responses. The positive predictive value was calculated to be 1.0 (11 ÷ 11); 95% confidence intervals, 1.0, 1.0.
4. Negative Predictive Value: Non-amenable mutant forms were represented in 5 male patients. None of the 5 patients showed positive plasma lyso-Gb_3 responses. The negative predictive value was calculated to be 1.0 (5 ÷ 5); 95% confidence intervals, 1.0, 1.0.

Figure 1S: GLP HEK assay Procedure



The GLP HEK assay includes: 1. Plasmid DNA quality control assessments and storage specifications; 2. Binary design in which *GLA* transfected HEK cells are incubated in the absence or presence of a 10 µM migalastat (AT1001); 3. Quantitative real-time PCR transfection efficiency control obtained from every sample; 4. Consistent assay acceptance criteria.

Figure 2S: Mutant α-Gal A Responses in the GLP HEK Assay



Migalastat increases the activity of different α-Gal A mutant forms. Six hundred (600) mutant forms were evaluated in the GLP HEK assay for increases in α-Gal A activity in response to incubation with 10 µM migalastat. The average baseline (orange bars) and average increased (blue bars) α-Gal A activity in the absence or presence of migalastat, respectively, are shown. The data have been normalized to the α-Gal A activity of untreated wild-type. Mutant forms with no associated bar did not have any quantifiable baseline α-Gal A activity nor response to migalastat.

Table 1S: Effect of Migalastat on Mutant α-Gal A Activity Measured in HEK-293 Cell Lysates

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	Nucleotide Change	α-Gal A Activity (nmol/mg/hr)	% WT	α-Gal A Activity (nmol/mg/hr)	% WT			
M1I	c.3 G>A	159 ± 12	0.5 ± 0.0	186 ± 31	0.6 ± 0.1	0.1	1.17	no
M1K	c.2 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
M1L	c.1 A>C	186 ± 16	0.6 ± 0.1	268 ± 35*	0.8 ± 0.1	0.3	1.44	no
M1R	c.2 T>G	BLD	N/A	219 ± 25**	0.6 ± 0.1	0.6	NC	no
M1T	c.2 T>C	187 ± 15	0.5 ± 0.0	234 ± 30*	0.7 ± 0.1	0.1	1.26	no
M1V	c.1 A>G	BLD	N/A	166 ± 29	0.5 ± 0.1	0.5	NC	no
L3P	c.8 T>C	24582 ± 1394	71.9 ± 4.5	31557 ± 1312***	92.2 ± 4.5	20.3	1.28	yes
C12_L14del-3aa or 12del3aa or 12del3	c.34 del TGCGCGCTT	934 ± 32	2.7 ± 0.1	1245 ± 47***	3.6 ± 0.1	0.9	1.33	no
A13P	c.37 G>C	1952 ± 136	5.6 ± 0.4	5102 ± 140***	14.9 ± 0.6	9.3	2.61	yes
A13T	c.37G>A	17810 ± 823	51.7 ± 2.5	21391 ± 849**	62.2 ± 2.6	10.4	1.20	yes
L14P	c.41 T>C	BLD	N/A	183 ± 29*	0.5 ± 0.1	0.5	NC	no
A15G	c.44 C>G	7293 ± 437	19 ± 0.7	10647 ± 594***	28 ± 1.2	9.0	1.46	yes
A15P	c.43 G>C	328 ± 22	0.9 ± 0	462 ± 37**	1.2 ± 0.1	0.3	1.41	no
A15T	c.43 G>A	12581 ± 757	39.1 ± 1.3	18353 ± 851***	57.5 ± 1.4	18.4	1.46	yes
L16H	c.47 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
L16P	c.47 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
F18S	c.53 T>C	699 ± 29	2.0 ± 0.1	897 ± 44***	2.5 ± 0.1	0.5	1.28	no
19del-5aa	c.57 Del GCCCTCGTTTCCTGG	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
L19P	c.56 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L19Q	c.56 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
A20D	c.59 C>A	1625 ± 68	4.3 ± 0.2	3864 ± 346***	10 ± 0.8	5.7	2.38	yes
A20P	c.58 G>C	3955 ± 238	11.5 ± 0.8	5483 ± 352**	15.9 ± 1.1	4.4	1.39	yes
A20V	c.59 C>T	29269 ± 1385	81.7 ± 3.7	30693 ± 1277	86.1 ± 3.6	4.4	1.05	no
L21F	c.61C>T	25529 ± 1105	71.4 ± 2.9	27062 ± 1039	75.9 ± 3.0	4.5	1.06	no
L21P	c.62 T>C	380 ± 28	1.1 ± 0.1	549 ± 36***	1.6 ± 0.1	0.5	1.44	no
L21R	c.62 T>G	419 ± 40	1.2 ± 0.1	640 ± 44***	1.8 ± 0.1	0.6	1.53	no
W24C	c.72 G>C	6711 ± 373	19.9 ± 1.2	11951 ± 534***	35.0 ± 1.3	15.1	1.78	yes
W24G	c.70 T>G	8723 ± 855	22.1 ± 1.1	15839 ± 950***	41 ± 1.1	19.0	1.82	yes
W24R	c.70 T>A	20250 ± 1395	52.6 ± 2.3	24519 ± 1565**	63.4 ± 1.7	10.9	1.21	yes
A31V	c.92 C>T	593 ± 35	1.7 ± 0.1	1030 ± 29***	3.0 ± 0.1	1.3	1.74	no
L32P	c.95 T>C	2529 ± 183	7.3 ± 0.4	12391 ± 735***	36.3 ± 2.0	29.0	4.90	yes
D33G	c.98 A>G	9913 ± 600	29.3 ± 1.8	24033 ± 865***	70.6 ± 2.4	41.3	2.42	yes
D33Y	c.97 G>T	6209 ± 465	18.0 ± 1.2	16998 ± 723***	49.6 ± 1.7	31.7	2.74	yes
N34K	c.102 T>A	BLD	N/A	2231 ± 196***	6.6 ± 0.6	6.6	NC	yes
N34S	c.101 A>G	195 ± 35	0.6 ± 0.1	5690 ± 239***	16.7 ± 0.6	16.1	29.23	yes
G35R	c.103 G>A	6400 ± 321	19.2 ± 1.0	22376 ± 1529***	66.1 ± 3.4	46.9	3.50	yes
L36F	c.108 G>C	1305 ± 75	4.0 ± 0.3	12093 ± 753***	35.9 ± 1.7	31.9	9.27	yes
L36S	c.107 T>C	10811 ± 481	32.5 ± 1.6	25401 ± 1000***	76.9 ± 3.8	44.3	2.35	yes
L36W	c.107 T>G	241 ± 19	0.7 ± 0.1	5182 ± 463***	16.6 ± 2.1	15.9	21.49	yes
A37T	c.109 G>A	16336 ± 625	48.9 ± 1.8	32066 ± 1226***	96.4 ± 3.9	47.5	1.96	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
A37V	c.110 C>T	15709 ± 855	46.7 ± 2.0	24997 ± 1355***	75.1 ± 3.9	28.4	1.59	yes
P40A	c.118 C>G	BLD	N/A	775 ± 43***	2.1 ± 0.1	2.1	NC	no
P40H	c.119 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
P40L	c.119 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
P40R	c.119 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
P40S	c.118 C>T	BLD	N/A	308 ± 26***	1.0 ± 0.1	1.0	NC	no
T41I	c.122 C>T	22348 ± 897	68.7 ± 3.1	37401 ± 1677***	116.7 ± 7.1	48.0	1.67	yes
M42K	c.125 T>A	1284 ± 39	3.9 ± 0.1	9851 ± 505***	29.7 ± 1.5	25.8	7.67	yes
M42L	c.124 A>C	12287 ± 726	38.8 ± 2.0	18812 ± 893***	60.2 ± 2.7	21.3	1.53	yes
M42R	c.125 T>G	2262 ± 231	6.9 ± 0.4	9236 ± 336***	29.5 ± 1.0	22.7	4.08	yes
M42T	c.125 T>C	788 ± 44	2.5 ± 0.1	6287 ± 328***	20.3 ± 1.2	17.8	7.98	yes
M42V	c.124 A>G	159 ± 20	0.5 ± 0.1	1338 ± 52***	4.3 ± 0.1	3.8	8.44	yes
G43D	c.128 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G43R	c.127 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
G43S	c.127 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G43V	c.128 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W44C	c.132 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
L45P	c.134 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L45R	c.134 T>G	224 ± 23	0.6 ± 0.1	194 ± 22	0.6 ± 0.1	-0.1	0.87	no
L45R/H46S	c.134_138 del TGCAC; ins GCTCG	BLD	N/A	BLD	N/A	N/A	N/A	no
H46L	c.137 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
H46P	c.137 A>C	10645 ± 580	31.0 ± 1.2	36121 ± 1306***	106.9 ± 4.4	75.9	3.39	yes
H46R	c.137 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
H46Y	c.136 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W47C	c.141 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W47G	c.139 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
W47L	c.140 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W47R	c.139 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
E48D	c.144 G>T	177 ± 17	0.5 ± 0.0	741 ± 40***	2.0 ± 0.1	1.5	4.17	no
E48K	c.142 G>A	260 ± 18	0.9 ± 0.1	402 ± 23***	1.3 ± 0.1	0.5	1.54	no
E48Q	c.142 G>C	844 ± 40	2.3 ± 0.1	4481 ± 151***	12.0 ± 0.4	9.7	5.31	yes
49insP-1aa or 49ins1	c.147_148 Ins CCC	BLD	N/A	BLD	N/A	N/A	N/A	no
R49C	c.145 C>T	BLD	N/A	1031 ± 71***	2.7 ± 0.2	2.7	NC	no
R49G	c.145 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
R49L	c.146 G>T	BLD	N/A	332 ± 43***	0.9 ± 0.1	0.9	NC	no
R49P	c.146 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
R49S	c.145 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
F50C	c.149 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
M51I	c.153 G>A	9074 ± 557	22.3 ± 1.1	19030 ± 676***	47.1 ± 1.5	24.7	2.10	yes
M51K	c.152 T>A	2020 ± 137	6.3 ± 0.5	6950 ± 360***	22.1 ± 1.9	15.8	3.44	yes
C52G	c.154 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C52R	c.154 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
C52S	c.155 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C52W	c.156 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C52Y	c.155 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
N53D	c.157 A>G	17104 ± 863	42.2 ± 1.9	32019 ± 821***	79.4 ± 2.0	37.2	1.87	yes
N53L	c.157 A>C; c.158 A>T	7509 ± 460	18.5 ± 0.9	19650 ± 762***	48.6 ± 1.5	30.1	2.62	yes
L54F	c.160 C>T	1796 ± 87	5 ± 0.2	15077 ± 875***	41.4 ± 1.4	36.5	8.39	yes
L54P	c.161 T>C	BLD	N/A	4589 ± 296***	11.2 ± 0.5	11.2	NC	yes
D55V[φ]	c.164 A>T	176 ± 27	0.5 ± 0.1	6566 ± 454***	19.1 ± 1.0	18.5	37.34	yes
D55V/Q57L	c.164 A>T; c.170 A>T	BLD	N/A	2526 ± 287***	8.0 ± 0.5	8.0	NC	yes
C56F	c.167 G>T	BLD	N/A	2195 ± 261***	6.4 ± 0.7	6.4	NC	yes
C56G	c.166 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C56S	c.167 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C56Y	c.167 G>A	BLD	N/A	2517 ± 271***	7.3 ± 0.7	7.3	NC	yes
Q57L[φ]	C170 A>T	24215 ± 725	71.6 ± 2.0	31563 ± 1022***	93.3 ± 2.7	21.7	1.30	yes
E59K	c.175 G>A	2910 ± 192	8.6 ± 0.5	5861 ± 230***	17.5 ± 0.8	9.0	2.01	yes
P60L	c.179 C>T	7464 ± 483	21.7 ± 1.1	20863 ± 1170***	61.0 ± 2.4	39.2	2.80	yes
P60S	c.178 C>T	13236 ± 1201	35.1 ± 1.7	28850 ± 1909***	78.1 ± 2	43.0	2.18	yes
P60T	c.178 C>A	9459 ± 792	25.3 ± 1.3	28325 ± 1457***	77.7 ± 1.9	52.4	2.99	yes
C63R	c.187 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C63S	c.188 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C63Y	c.188 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
E66G	c.197 A>G	12137 ± 377	34.2 ± 1.0	16474 ± 746***	46.2 ± 1.7	11.9	1.36	yes
E66K	c.196 G>A	1694 ± 51	4.8 ± 0.1	4462 ± 171***	12.9 ± 0.8	8.1	2.63	yes
E66Q	c.196 G>C	18508 ± 569	52.0 ± 1.3	19720 ± 1005	55.0 ± 2.1	3.0	1.07	no
L68F	c.202 C>T	BLD	N/A	278 ± 38***	0.8 ± 0.1	0.8	NC	no
M72I	c.216 G>A	19494 ± 758	54.7 ± 1.8	27499 ± 929***	77.6 ± 2.6	22.8	1.41	yes
M72R	c.215 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
M72V	c.214 A>G	5090 ± 261	14.5 ± 0.9	26104 ± 831***	73.2 ± 1.3	58.7	5.13	yes
A73E	c.218 C>A	203 ± 26	0.5 ± 0	522 ± 47***	1.4 ± 0.1	0.9	2.57	no
A73V	c.218 C>T	18892 ± 383	53.6 ± 1.6	30798 ± 701***	86.9 ± 2.1	33.3	1.63	yes
M76R	c.227 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
M76T	c.227 T>C	1047 ± 33	2.7 ± 0.1	4722 ± 187***	12.2 ± 0.7	9.6	4.51	yes
W81C	c.243 G>T	BLD	N/A	288 ± 15***	0.7 ± 0.0	0.7	NC	no
W81R	c.241 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
W81S	c.242 G>C	BLD	N/A	179 ± 20***	0.6 ± 0.1	0.6	NC	no
D83N	c.247G>A	26837 ± 844	69.2 ± 3.3	36340 ± 1231***	93.0 ± 3.7	23.9	1.35	yes
G85D	c.254 G>A	888 ± 38	2.7 ± 0.1	4534 ± 135***	14.3 ± 0.9	11.6	5.10	yes
G85M	c.253 G>A; c.254 G>T; c.255 T>G	3148 ± 261	7.9 ± 0.5	4680 ± 338**	11.8 ± 0.7	4.0	1.49	yes
G85S	c.253 G>A	4914 ± 361	12.4 ± 0.8	7431 ± 217***	19.1 ± 0.8	6.7	1.51	yes
86del6 or 86del-6aa	c.258del18 GAG TAC CTC TGC ATT GAT	BLD	N/A	BLD	N/A	N/A	N/A	no
Y86C	c.257 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
Y86D	c.256 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
Y86H	c.256 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
Y88D	c.262 T>G	BLD	N/A	399 ± 18***	1.0 ± 0.0	1.0	NC	no
L89F	c.265 C>T	6990 ± 491	18.9 ± 0.8	13716 ± 689***	37.8 ± 1.1	18.9	1.96	yes
L89P	c.266 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L89R	c.266 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C90R	c.268 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C90Y	c.269 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
I91T	c.272 T>C	372 ± 19	0.9 ± 0.1	5227 ± 293***	12.6 ± 0.5	11.6	14.07	yes
D92G	c.275 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
D92H	c.274 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
D92N	c.274 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D92V	c.275A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D92Y	c.274 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D93E	c.279 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
D93G	c.278 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
D93N	c.277 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D93V	c.278 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D93Y	c.277 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
C94S	c.281 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C94Y	c.281 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
W95L	c.284 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
W95S	c.284 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
M96I	c.288 G>A	10088 ± 549	30.3 ± 1.2	19384 ± 1082***	58.2 ± 2.5	27.9	1.92	yes
A97P	c.289 G>C	245 ± 16	0.7 ± 0.0	1443 ± 62***	4.0 ± 0.1	3.3	5.88	yes
A97V	c.290 C>T	3854 ± 118	12.2 ± 0.8	12772 ± 548***	39.6 ± 2.3	27.4	3.31	yes
R100K	c.299 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
R100T	c.299 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
S102L	c.305 C>T	6645 ± 500	19.9 ± 1	20794 ± 1141***	62.8 ± 2.2	42.9	3.13	yes
E103Q	c.307 G>C	36955 ± 1623	102.9 ± 3.7	41654 ± 2285	114.6 ± 3.9	11.7	1.13	no
G104V	c.311G>T	7506 ± 378	20.9 ± 0.8	12067 ± 506***	33.6 ± 1.1	12.8	1.61	yes
L106R	c.317 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
Q107L	c.320 A>T	35023 ± 1291	98.4 ± 4.3	39620 ± 1540*	110.0 ± 2.7	11.6	1.13	no
A108T	c.322 G>A	20760 ± 1166	57.1 ± 2.2	29391 ± 1630***	80.8 ± 2.9	23.7	1.42	yes
D109G	c.326 A>G	863 ± 62	2.6 ± 0.1	3384 ± 188***	10.3 ± 0.5	7.7	3.92	yes
R112C	c.334 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
R112G	c.334 C>G	BLD	N/A	1219 ± 41***	3.5 ± 0.2	3.5	NC	yes
R112H	c.335 G>A	845 ± 39	2.6 ± 0.1	5583 ± 215***	17.4 ± 0.8	14.8	6.61	yes
R112S	c.334 C>A	BLD	N/A	1109 ± 53***	2.8 ± 0.2	2.8	NC	no
113del6 or del113-6	c.336 Del TTTCCTCATGG GATTCGC	BLD	N/A	BLD	N/A	N/A	N/A	no
F113L	c.337 T>C	7327 ± 399	18.3 ± 0.8	16382 ± 637***	41.2 ± 1.5	22.9	2.24	yes
F113S	c.338 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
I117S	c.350 T>G	288 ± 18	0.7 ± 0.0	598 ± 36***	1.5 ± 0.1	0.8	2.08	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
R118C	c.352 C>T	9544 ± 529	24.0 ± 1.3	11903 ± 555**	29.5 ± 0.7	5.5	1.25	yes
L120H-del-2aa or L120H-del2	c.358 Del6 ntd TAGCTA	BLD	N/A	BLD	N/A	N/A	N/A	no
L120P	c.359 T>C	BLD	N/A	199 ± 19***	0.5 ± 0.0	0.5	NC	no
L120P/A121T	c.359 T>C; c.361 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
L120S	c.358 C>T; c.359 T>C	BLD	N/A	922 ± 39***	2.4 ± 0.1	2.4	NC	no
L120V	c.358 C>G	26234 ± 869	66.8 ± 3.1	29802 ± 1234*	74.7 ± 2.4	7.9	1.14	no
A121P	c.361 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A121T	c.361 G>A	5292 ± 184	18.9 ± 0.5	18850 ± 721***	67.9 ± 3.4	49.0	3.56	yes
Y123C	c.368 A>G	2932 ± 190	8.9 ± 0.4	5084 ± 335***	15.1 ± 0.5	6.3	1.73	yes
V124D	c.371 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
H125L	c.374 A>T	563 ± 27	1.4 ± 0.1	1947 ± 187***	4.7 ± 0.4	3.3	3.46	yes
H125L/G128E	c.374 A>T; c.383 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
H125P	c.374 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
S126G	c.376 A>G	34476 ± 1611	83.7 ± 2.4	46491 ± 1720***	113.9 ± 3.2	30.2	1.35	yes
G128E	c.383 G>A	17297 ± 1047	45.2 ± 1.8	22334 ± 1057**	58.5 ± 1.7	13.4	1.29	yes
L129P	c.386 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
K130R	c.389 A>G	24226 ± 1579	63.0 ± 2.7	28327 ± 1972	73.7 ± 3.9	10.7	1.17	no
L131P	c.392 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
G132A	c.395 G>C	BLD	N/A	774 ± 66***	2.5 ± 0.1	2.5	NC	no
G132E	c.395 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
G132R	c.394 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
Y134D	c.400 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
Y134H	c.400 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
Y134S	c.401 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A135V	c.404 C>T	BLD	N/A	1397 ± 36***	3.7 ± 0.1	3.7	NC	yes
D136E	c.408 T>A	545 ± 21	1.4 ± 0.1	4958 ± 195***	12.9 ± 0.8	11.5	9.10	yes
D136H	c.406 G>C	628 ± 27	1.6 ± 0.1	1565 ± 56***	4.0 ± 0.2	2.4	2.49	no
D136Y	c.406 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
G138E	c.413 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G138R	c.412 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
N139S	c.416 A>G	25805 ± 1183	65.5 ± 2.0	31068 ± 1539**	79.1 ± 3.2	13.6	1.20	yes
N139T	c.416 A>C	27948 ± 1068	71.4 ± 2.2	31174 ± 1204*	79.4 ± 2.0	7.9	1.12	no
K140T	c.419 A>C	17228 ± 1211	51.4 ± 2.1	30034 ± 1847***	89.8 ± 2.7	38.4	1.74	yes
T141I	c.422 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
T141N	c.422 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
C142R	c.424 T>C	182 ± 19	0.4 ± 0.0	BLD	N/A	N/A	N/A	no
C142W	c.426 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C142Y	c.425 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
A143P	c.427 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A143T	c.427 G>A	6874 ± 248	21.4 ± 0.8	14038 ± 309***	43.8 ± 1.4	22.4	2.04	yes
G144D	c.431 G>A	16773 ± 1140	50.2 ± 2.2	25424 ± 1311***	76.5 ± 1.7	26.3	1.52	yes
G144V	c.431 G>T	253 ± 21	0.8 ± 0.1	2924 ± 335***	9.2 ± 1.2	8.4	11.58	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
P146S	c.436 C>T	16859 ± 910	41.9 ± 1.9	25622 ± 1398***	64.1 ± 3.7	22.2	1.52	yes
G147E	c.440 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G147R	c.439 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
S148N	c.443 G>A	BLD	N/A	273 ± 16***	0.7 ± 0.0	0.7	NC	no
S148R	c.444 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
152ins-D-aa or 152insD or 152ins	c.455_456 CGA insertion	BLD	N/A	BLD	N/A	N/A	N/A	no
Y152C	c.455 A>G	6934 ± 250	16.7 ± 0.6	13163 ± 696***	31.5 ± 1.4	14.8	1.90	yes
153del or del153aa	c.456 DelGAC	BLD	N/A	BLD	N/A	N/A	N/A	no
D155H	c.463 G>C	BLD	N/A	579 ± 30***	1.4 ± 0.1	1.4	NC	no
A156D	c.467 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
A156T	c.466 G>A	907 ± 31	2.8 ± 0.1	7034 ± 289***	21.9 ± 0.9	19.1	7.75	yes
A156V	c.467 C>T	505 ± 25	1.2 ± 0.1	5340 ± 315***	12.8 ± 0.7	11.6	10.58	yes
W162C	c.486 G>C	188 ± 20	0.5 ± 0.1	BLD	N/A	N/A	N/A	no
W162G	c.484 T>G	338 ± 26	0.8 ± 0.1	2538 ± 222***	5.9 ± 0.4	5.1	7.50	yes
W162L	c.485 G>T	BLD	N/A	BLD	N/A	N/A	N/A	No
W162R	c.484 T>C	BLD	N/A	456 ± 22***	1.1 ± 0.1	1.1	NC	no
G163V	c.488 G>T	458 ± 30	1.4 ± 0.1	969 ± 45***	2.9 ± 0.1	1.5	2.12	no
V164G	c.491 T>G	558 ± 49	1.7 ± 0.1	1061 ± 64***	3.2 ± 0.1	1.5	1.90	no
D165G	c.494 A>G	808 ± 21	2.5 ± 0.1	4414 ± 275***	13 ± 0.4	10.5	5.46	yes
D165H	c.493 G>C	448 ± 34	1.3 ± 0.1	2869 ± 365***	8.3 ± 0.9	7.0	6.40	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
D165V	c.494 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D165Y	c.493 G>T	BLD	N/A	428 ± 26***	1.3 ± 0.1	1.3	NC	no
L166G	c.496 C>G; c.497 T>G	3478 ± 279	10.2 ± 0.6	11075 ± 627***	33.0 ± 1.6	22.8	3.18	yes
L166V	c.496 C>G	1306 ± 100	3.8 ± 0.2	7069 ± 447***	20.9 ± 1.1	17.1	5.41	yes
L167P	c.500 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L167Q	c.500 T>A	BLD	N/A	186 ± 16***	0.6 ± 0.1	0.6	NC	No
K168N	c.504 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
K168R	c.503 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
F169S	c.506 T>C	4375 ± 594	12.8 ± 1.4	26078 ± 1758***	78.7 ± 3.8	65.9	5.96	yes
D170G	c.509 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
D170H	c.508 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
D170N	c.508 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D170V	c.509 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
G171C	c.511 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
G171D	c.512 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G171R	c.511 G>C	1628 ± 83	4.9 ± 0.2	2190 ± 246	6.4 ± 0.5	1.4	1.35	no
C172F	c.515 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
C172G	c.514 T>G	349 ± 24	1.1 ± 0.1	881 ± 60***	2.7 ± 0.2	1.6	2.53	no
C172R	c.514 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C172S	c.515 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C172W	c.516 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
C172Y	c.515 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
C174G	c.520 T>G	10655 ± 475	29.6 ± 1.5	33198 ± 2150***	91.2 ± 5.2	61.6	3.12	yes
C174R	c.520 T>C	4671 ± 270	14.3 ± 0.6	16505 ± 393***	51.6 ± 2.0	37.4	3.53	yes
D175E	c.525 C>G	15726 ± 1126	44.3 ± 2.9	18946 ± 953*	53.4 ± 2	9.1	1.20	yes
G183A	c.548 G>C	8094 ± 665	22.4 ± 1.9	20538 ± 1068***	56.4 ± 2.7	34.0	2.54	yes
G183D	c.548 G>A	207 ± 15	0.7 ± 0.1	6074 ± 212***	19.1 ± 1.0	18.4	29.31	yes
G183V	c.548 G>T	BLD	N/A	796 ± 29***	2.5 ± 0.1	2.5	NC	no
Y184C	c.551A>G	609 ± 37	1.7 ± 0.1	2667 ± 318***	7.2 ± 0.8	5.6	4.38	yes
Y184N	c.550 T>A	831 ± 80	2.3 ± 0.2	3445 ± 380***	9.7 ± 1	7.4	4.15	yes
K185E	c.553 A>G	14363 ± 1097	39.6 ± 3.1	25849 ± 1110***	71.3 ± 2.9	31.8	1.80	yes
H186P	c.557 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
M187I	c.561 G>A	1775 ± 57	5.1 ± 0.2	10824 ± 555***	30.7 ± 1.1	25.6	6.10	yes
M187R	c.560 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
M187S188ins or 187del2aa	c.565 Ins ATGTCC	488 ± 53	1.2 ± 0.1	3434 ± 466***	8.6 ± 1.1	7.4	7.04	yes
M187T	c.560 T>C	3548 ± 354	9.8 ± 1.0	9900 ± 644***	27.4 ± 1.8	17.7	2.79	yes
M187V	c.559 A>G	7318 ± 565	20.1 ± 1.5	16628 ± 1075***	45.7 ± 2.8	25.6	2.27	yes
L191P	c.572 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L191Q	c.572 T>A	234 ± 16	0.6 ± 0.0	3616 ± 512***	9.0 ± 1.2	8.4	15.45	yes
T194I	c.581 C>T	908 ± 56	2.3 ± 0.1	7563 ± 578***	19.1 ± 1.2	16.8	8.33	yes
G195V	c.584 G>T	7154 ± 228	25.8 ± 1.3	13437 ± 383***	48.2 ± 1.5	22.3	1.88	yes
I198T	c.593 T>C	25662 ± 1774	64.7 ± 3.5	38048 ± 2670***	95.5 ± 4.8	30.8	1.48	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
V199G	c.596 T>G	10219 ± 842	26.0 ± 1.9	24502 ± 1693***	62.7 ± 3.8	36.6	2.40	yes
V199M	c.595 G>A	23234 ± 1550	59.7 ± 3.8	42207 ± 1690***	108.4 ± 3.9	48.6	1.82	yes
Y200C	c.599 A>G	521 ± 24	1.3 ± 0.1	5910 ± 421***	14.9 ± 0.9	13.6	11.35	yes
S201F	c.602 C>T	911 ± 42	2.4 ± 0.1	11996 ± 876***	30.8 ± 1.8	28.4	13.16	yes
S201Y	c.602 C>A	2524 ± 148	6.5 ± 0.3	15727 ± 995***	40.2 ± 1.7	33.6	6.23	yes
C202R	c.604 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C202R/N215S	c.604 T>C; c.644 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C202W	c.606 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C202Y	c.605 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
E203D	c.609 G>C	1271 ± 108	3.4 ± 0.1	3353 ± 336***	9 ± 0.6	5.6	2.64	yes
E203K	c.607 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
E203V	c.608 A>T	16830 ± 1210	43.0 ± 2.4	24921 ± 1228***	64.5 ± 2.4	21.5	1.48	yes
W204C	c.612 G>T	BLD	N/A	427 ± 37***	1.1 ± 0.1	1.1	NC	no
205del3 or del205-7 or 205del3aa	c.612 Del9 CCTCTTTAT	BLD	N/A	BLD	N/A	N/A	N/A	no
P205L	c.614 C>T	258 ± 18	0.8 ± 0.1	1633 ± 252***	4.7 ± 0.7	3.9	6.34	yes
P205R	c.614 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
P205S	c.613 C>T	12423 ± 1020	35.3 ± 2.2	32286 ± 2137***	93.2 ± 5.5	57.9	2.60	yes
P205T	c.613 C>A	4802 ± 230	14.4 ± 0.9	16371 ± 647***	48.8 ± 2.2	34.4	3.41	yes
L206P	c.617 T>C	BLD	N/A	230 ± 20***	0.7 ± 0.1	0.7	NC	no
Y207C	c.620 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
Y207H	c.619 T>C	11787 ± 617	34.4 ± 2.0	22407 ± 1029***	65.5 ± 3.2	31.1	1.90	yes
Y207S	c.620 A>C	766 ± 40	2.2 ± 0.1	2594 ± 315***	7.3 ± 0.8	5.1	3.39	yes
P210L	c.629 C>T	9895 ± 792	27.1 ± 1	21673 ± 1165***	60.5 ± 1.7	33.4	2.19	yes
P210S	c.628 C>T	27219 ± 1787	75.2 ± 2	40698 ± 2183***	113.3 ± 2.7	38.2	1.50	yes
K213M	c.638 A>T	15309 ± 722	43.2 ± 1.4	19904 ± 1061***	55.9 ± 1.8	12.7	1.30	yes
P214L	c.641 C>T	11857 ± 868	33 ± 1.3	32647 ± 1804***	91.6 ± 1.6	58.6	2.75	yes
P214S	c.640 C>T	7895 ± 555	22.4 ± 1.1	28745 ± 1688***	82.5 ± 3.8	60.1	3.64	yes
N215D	c.643 A>G	16980 ± 1644	43.8 ± 3.0	21987 ± 1391**	58.3 ± 3.1	14.5	1.29	yes
N215S	c.644 A>G	5154 ± 239	15.6 ± 1.0	11976 ± 334***	35.6 ± 1.2	20.0	2.32	yes
N215S/D313Y$^{\varphi}$	c.644 A>G; c.937 G>T	569 ± 47	1.5 ± 0.1	3678 ± 381***	9.7 ± 1.0	8.2	6.46	yes
N215S/G271S$^{\varphi}$	c.644 A>G; c.811 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
N215S/G271S/ D313Y$^{\varphi}$	c.644 A>G; c.811 G>A; c.937 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
Y216C	c.647 A>G	673 ± 38	2.0 ± 0.1	7003 ± 305***	20.7 ± 0.8	18.7	10.40	yes
Y216D	c.646 T>G	516 ± 50	1.6 ± 0.1	4233 ± 372***	13.3 ± 0.7	11.7	8.21	yes
I219N	c.656 T>A	242 ± 18	0.6 ± 0.1	4806 ± 396***	12.9 ± 1.1	12.2	19.87	yes
I219T	c.656 T>C	21564 ± 1710	55.8 ± 2.9	34880 ± 1199***	93.6 ± 3.7	37.8	1.62	yes
R220P	c.659 G>C	11244 ± 1052	30.9 ± 1.8	22597 ± 1382***	63.5 ± 2.2	32.6	2.01	yes
R220Q	c.660 G>A	16215 ± 1135	45.2 ± 1.4	21913 ± 1115***	61.7 ± 0.8	16.5	1.35	yes
C223G	c.667 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C223R	c.667 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
C223Y	c.668 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
N224D	c.670 A>G	BLD	N/A	997 ± 31***	2.7 ± 0.1	2.7	NC	no
N224S	c.671 A>G	3918 ± 371	10.3 ± 1.0	11625 ± 1244***	29.7 ± 2.8	19.4	2.97	yes
H225D	c.673 C>G	16595 ± 932	43.8 ± 2.6	42058 ± 2750***	110.6 ± 7.2	66.9	2.53	yes
H225R	c.674 A>G	BLD	N/A	687 ± 33***	2.0 ± 0.1	2.0	NC	no
W226C	c.678 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W226R	c.676 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
R227P	c.680 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
R227Q	c.680 G>A;	BLD	N/A	BLD	N/A	N/A	N/A	no
N228S	c.683 A>G	48389 ± 2790	124.5 ± 4.1	63268 ± 2078***	169.2 ± 8.2	44.7	1.31	yes
F229L	c.687 T>G	7760 ± 694	21.4 ± 1.1	13519 ± 885***	37.6 ± 0.8	16.2	1.74	yes
A230T	c.688 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D231G	c.692 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
D231N	c.691 G>A	187 ± 12	0.5 ± 0.0	BLD	N/A	N/A	N/A	no
D231V	c.692 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
I232T	c.695 T>C	6486 ± 826	15.0 ± 1.6	36389 ± 2899***	85.0 ± 4.1	69.9	5.61	yes
D234E	c.702 T>G	159 ± 19	0.4 ± 0.0	339 ± 28***	0.8 ± 0.1	0.4	2.13	no
D234Y	c.700 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
S235C	c.704 C>G	BLD	N/A	306 ± 58***	0.7 ± 0.1	0.7	NC	no
S235F	c.704 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
S235Y	c.704 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
W236C	c.708 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
W236L	c.707 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W236R	c.706 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
S238N	c.713 G>A	9330 ± 395	37.1 ± 1.8	24510 ± 777***	96.4 ± 2.0	59.3	2.63	yes
S238R	c.714 T>G	13999 ± 688	55.3 ± 2.7	14781 ± 758	58.0 ± 2.5	2.7	1.06	no
I239del or del-I239 or 239del or 239del1	c.715 del ATA	BLD	N/A	BLD	N/A	N/A	N/A	no
I239T	c.716 T>C	9473 ± 448	37.7 ± 1.9	23430 ± 954***	92.8 ± 3.9	55.2	2.47	yes
I242F	c.724 A>T	270 ± 15	1.1 ± 0.1	2253 ± 185***	9.0 ± 0.8	7.9	8.36	yes
I242N	c.725 T>A	1909 ± 57	7.6 ± 0.3	16871 ± 859***	67.4 ± 4.2	59.7	8.84	yes
L243F	c.729 G>C	2694 ± 117	7.9 ± 0.3	14370 ± 618***	42.3 ± 1.4	34.4	5.33	yes
L243W	c.728 T>G	190 ± 24	0.6 ± 0.1	4729 ± 227***	14.3 ± 0.9	13.7	24.86	yes
D244H	c.730 G>C	6129 ± 366	18.1 ± 1.1	14873 ± 425***	44.0 ± 1.3	25.9	2.43	yes
D244N	c.730 G>A	10317 ± 386	30.9 ± 1.6	16321 ± 402***	48.7 ± 1.7	17.8	1.58	yes
W245G	c.733 T>G	15737 ± 1100	44.1 ± 1.6	22218 ± 1097***	63 ± 1.4	18.9	1.41	yes
247ins3 or ins247-3aa	c.741 Ins TGGACATCT	BLD	N/A	476 ± 28***	1.8 ± 0.1	1.8	NC	no
S247C	c.740 C>G	7515 ± 308	28.0 ± 1.1	13828 ± 558***	51.5 ± 2.0	23.5	1.84	yes
S247P	c.739 T>C	BLD	N/A	351 ± 25***	1.3 ± 0.1	1.3	NC	no
N249K	c.747 C>A	6350 ± 649	17.9 ± 1.6	12325 ± 615***	35.2 ± 1.4	17.3	1.94	yes
Q250P	c.749 A>C	6647 ± 340	24.8 ± 1.3	15759 ± 786***	58.7 ± 2.9	33.9	2.37	yes
R252T	c.755 G>C	26643 ± 1720	74.8 ± 2.5	28168 ± 1724	79.1 ± 2.1	4.2	1.06	no
I253S	c.758 T>G	901 ± 55	3.3 ± 0.2	8374 ± 400***	31.2 ± 1.4	27.8	9.29	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
I253T	c.758 T>C	11287 ± 506	38.9 ± 3.0	23417 ± 1077***	80.2 ± 5.9	41.3	2.07	yes
254del or del254aa or 254del1	c.760-762 delGTT	9950 ± 504	37.2 ± 1.9	21123 ± 716***	78.7 ± 2.5	41.5	2.12	yes
A257D	c.770 C>A	BLD	N/A	271 ± 23***	1.0 ± 0.1	1.0	NC	no
A257G	c.770 C>G	15820 ± 749	59.0 ± 2.8	27273 ± 779***	101.7 ± 2.8	42.6	1.72	yes
A257P	c.769 G>C	4467 ± 329	16.6 ± 1.2	14040 ± 474***	52.3 ± 1.6	35.7	3.14	yes
G258R	c.772 G>C	9558 ± 348	32.6 ± 2.1	22630 ± 801***	78.1 ± 5.8	45.5	2.37	yes
G258V	c.773 G>T	1957 ± 86	7.7 ± 0.3	10126 ± 457***	39.8 ± 1.7	32.1	5.17	yes
P259L	c.776 C>T	2799 ± 190	10.9 ± 0.6	11189 ± 451***	44.0 ± 1.8	33.1	4.00	yes
P259R	c.776 C>G	6681 ± 364	23.3 ± 2.3	17645 ± 515***	60.3 ± 3.8	37.0	2.64	yes
G260A	c.779 G>C	2221 ± 142	7.5 ± 0.6	10749 ± 403***	37.4 ± 3.1	29.9	4.84	yes
G260E	c.779 G>A	3828 ± 318	10.6 ± 0.6	14341 ± 595***	41.1 ± 1.3	30.4	3.75	yes
G261D	c.782 G>A	BLD	N/A	590 ± 19***	2.1 ± 0.2	2.1	NC	no
G261V	c.782 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W262C	c.786 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
W262L	c.785 G>T	BLD	N/A	639 ± 35***	2.5 ± 0.1	2.5	NC	no
N263S	c.788 A>G	4010 ± 233	15.8 ± 0.9	20024 ± 998***	80.5 ± 6.2	64.8	4.99	yes
D264A	c.791 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
D264V	c.791 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D264Y	c.790 G>T	143 ± 13	0.5 ± 0.0	1842 ± 100***	6.2 ± 0.3	5.7	12.89	yes
D264Y/V269M	c.790 G>T; c.805 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
P265L	c.794 C>T	3510 ± 144	13.9 ± 0.7	19126 ± 837***	74.8 ± 2.9	60.9	5.45	yes
P265R	c.794 C>G	BLD	N/A	441 ± 18***	1.8 ± 0.1	1.8	NC	no
P265S	c.793 C>T	268 ± 16	1.0 ± 0.1	997 ± 38***	3.9 ± 0.2	2.8	3.73	no
D266A	c.797 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
D266E	c.798 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D266H	c.796 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
D266N	c.796 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
D266V	c.797 A>T	BLD	N/A	BLD	N/A	N/A	N/A	no
D266Y	c.796 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
M267R	c.800 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
M267T	c.800 T>C	9325 ± 374	28.8 ± 0.9	14708 ± 735***	45.3 ± 1.7	16.4	1.58	yes
L268S	c.803 T>C	BLD	N/A	715 ± 24***	2.8 ± 0.1	2.8	NC	no
V269A	c.806 T>C	BLD	N/A	1966 ± 137***	7.8 ± 0.7	7.8	NC	yes
V269E	c.806 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
V269M	c.805 G>A	1213 ± 40	4.4 ± 0.2	7170 ± 223***	25.9 ± 1.2	21.5	5.91	yes
I270T	c.809 T>C	1846 ± 119	6.3 ± 0.5	12416 ± 377***	42.8 ± 3.0	36.5	6.73	yes
G271C	c.811 G>T	BLD	N/A	156 ± 12***	0.5 ± 0.0	0.5	NC	no
G271D	c.812 G>A	477 ± 25	1.5 ± 0.1	10511 ± 778***	32.2 ± 2	30.8	22.06	yes
G271S	c.811 G>A	1329 ± 44	3.8 ± 0.1	11177 ± 520***	31.9 ± 1.3	28.1	8.41	yes
G271S/D313Y[φ]	c.811 G>A; c.937 G>T	BLD	N/A	877 ± 18***	3.0 ± 0.2	3.0	NC	yes
G271V	c.812 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
N272K	c.816 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
N272S	c.815 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
F273L	c.819 T>G	348 ± 13	1.3 ± 0.1	493 ± 19***	1.8 ± 0.1	0.5	1.42	no
G274S	c.820 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G274V	c.821 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
L275F	c.823 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
S276G	c.826 A>G	BLD	N/A	694 ± 25***	2.0 ± 0.1	2.0	NC	no
S276N	c.827 G>A	638 ± 18	2.3 ± 0.1	2511 ± 190***	9.3 ± 0.9	7.0	3.93	yes
W277C	c.831 G>C	9174 ± 479	28.5 ± 1.4	17288 ± 588***	53.7 ± 1.5	25.3	1.88	yes
W277G	c.829 T>G	16576 ± 1205	50.3 ± 2.2	27884 ± 1783***	84.9 ± 2.8	34.6	1.68	yes
Q279E	c.835 C>G	4865 ± 298	16.7 ± 1.0	14893 ± 507***	51.7 ± 2.2	35.0	3.06	yes
Q279H	c.837 G>C	BLD	N/A	152 ± 15***	0.5 ± 0.1	0.5	NC	no
Q279K	c.835 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
Q279R	c.836 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
Q280H	c.840 A>T	2119 ± 98	7.3 ± 0.4	11351 ± 594***	39.2 ± 2.1	31.8	5.36	yes
Q280K	c.838 C>A	8019 ± 395	27.7 ± 1.4	14012 ± 476***	48.5 ± 1.9	20.8	1.75	yes
V281A-del-1	c.841 DelTAA	BLD	N/A	BLD	N/A	N/A	N/A	no
T282A	c.844 A>G	BLD	N/A	1199 ± 38***	4.2 ± 0.2	4.2	NC	yes
T282I	c.845 C>T	1515 ± 57	5.2 ± 0.2	6918 ± 239***	23.7 ± 0.6	18.5	4.57	yes
T282N	c.845 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
Q283P	c.848 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
Q283R	c.848 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
M284T	c.851 T>C	606 ± 40	1.7 ± 0.1	5050 ± 268***	14.3 ± 0.6	12.6	8.33	yes
M284V	c.850 A>G	8003 ± 785	25.2 ± 1.6	19455 ± 970***	63.1 ± 2.4	37.9	2.43	yes
A285D	c.854 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
A285P	c.853 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
W287C	c.861 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
W287G	c.859 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
A288D	c.863 C>A	BLD	N/A	626 ± 26***	2.1 ± 0.1	2.1	NC	no
A288P	c.862 G>C	366 ± 26	1.1 ± 0.1	3541 ± 277***	10.4 ± 0.7	9.3	9.69	yes
I289F	c.865 A>T	BLD	N/A	246 ± 19***	0.8 ± 0.1	0.8	NC	no
I289S	c.866 T>G	BLD	N/A	795 ± 28***	3.0 ± 0.2	3.0	NC	yes
M290I	c.870 G>C	18049 ± 690	68.0 ± 3.4	30322 ± 1225***	114.8 ± 6.3	46.7	1.68	yes
M290L	c.868 A>C	15488 ± 629	58.6 ± 3.2	29261 ± 1572***	111.4 ± 7.7	52.8	1.89	yes
A291T	c.871 G>A	4401 ± 380	16.5 ± 1.5	10511 ± 768***	40.5 ± 3.8	24.0	2.39	yes
A292P	c.874 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A292T	c. 874 G>A	BLD	N/A	803 ± 22***	2.3 ± 0.1	2.3	NC	no
A292V	c.875 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
P293A	c.877 C>G	BLD	N/A	184 ± 18***	0.7 ± 0.1	0.7	NC	no
P293H	c.878 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
P293L	c.878 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
P293S	c.877 C>T	BLD	N/A	150 ± 15***	0.5 ± 0.0	0.5	NC	no
P293T	c.877 C>A	229 ± 20	0.7 ± 0.1	4488 ± 327***	13.3 ± 1.1	12.7	19.60	yes
L294S	c.881 T>C	BLD	N/A	1268 ± 37***	4.9 ± 0.1	4.9	NC	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
F295C	c.884 T>G	1196 ± 38	3.4 ± 0.1	5051 ± 190***	14.5 ± 0.6	11.1	4.22	yes
M296I	c.888 G>A	4036 ± 141	15.7 ± 0.7	16247 ± 1022***	63.2 ± 4.2	47.4	4.03	yes
M296L	c.886 A>C	3594 ± 164	14.0 ± 0.8	16728 ± 992***	65.4 ± 4.3	51.4	4.65	yes
M296T	c.887 T>C	427 ± 26	1.6 ± 0.1	6911 ± 722***	26.9 ± 2.9	25.3	16.18	yes
M296V	c.886 A>G	2896 ± 136	11.3 ± 0.6	14022 ± 852***	55.4 ± 4.4	44.1	4.84	yes
S297C	c.890 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
S297F	c.890 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
N298H	c.892 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
N298K	c.894 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
N298S	c.893 A>G	1610 ± 107	5.0 ± 0.2	13414 ± 892***	41.4 ± 1.5	36.4	8.33	yes
D299E	c.897 C>G	11248 ± 786	34.2 ± 1.5	23786 ± 1332***	73 ± 2.8	38.7	2.11	yes
D299G	c.896 A>G	BLD	N/A	BLD	N/A	N/A	N/A	no
L300F	c.898 C>T	4746 ± 363	14.8 ± 0.9	16129 ± 810***	50.5 ± 1.4	35.7	3.40	yes
L300H	c.899 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
L300P	c.899 T>C	1277 ± 38	3.7 ± 0.1	13219 ± 412***	37.9 ± 1.2	34.2	10.35	yes
R301G	c.901 C>G	5974 ± 309	19.1 ± 1.2	20713 ± 1192***	64.7 ± 2.1	45.6	3.47	yes
R301L	c.902 G>T	1369 ± 94	4.3 ± 0.2	11612 ± 602***	36.1 ± 0.7	31.9	8.48	yes
R301P	c.902 G>C	BLD	N/A	1440 ± 236***	4.2 ± 0.5	4.2	NC	yes
R301Q	c.902 G>A	1914 ± 52	5.5 ± 0.2	15547 ± 353***	44.5 ± 1.0	39.0	8.12	yes
I303N	c.908 T>A	BLD	N/A	2070 ± 180***	6.2 ± 0.3	6.2	NC	yes
S304N	c.911 G>A	30563 ± 1196	94.1 ± 1.1	39629 ± 1765***	121.8 ± 2.2	27.7	1.30	yes
S304T	c.911 G>C	23174 ± 1016	76.4 ± 1.6	35071 ± 1111***	116.9 ± 3.3	40.5	1.51	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
A307T	c.919 G>A	12581 ± 782	36.2 ± 1.2	30323 ± 1339***	87.7 ± 1.5	51.5	2.41	yes
K308N	c.924 A>C	1331 ± 123	3.7 ± 0.2	6219 ± 476***	17.6 ± 0.8	13.9	4.67	yes
A309P	c.925 G>C	313 ± 24	0.9 ± 0.1	3599 ± 352***	10.0 ± 0.6	9.1	11.51	yes
L310F	c.928 C>T	300 ± 41	0.8 ± 0.1	4270 ± 554***	11.6 ± 1.2	10.8	14.23	yes
L310R	c.929 T>G	BLD	N/A	242 ± 18***	0.7 ± 0.0	0.7	NC	no
L311F	c.931 C>T	BLD	N/A	596 ± 32***	2 ± 0.1	2.0	NC	no
L311P	c.932 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
L311R	c.932 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
L311V	c.931 C>G	598 ± 34	2 ± 0.1	5434 ± 286***	18 ± 0.8	16.0	9.09	yes
Q312H	c.936 G>C	2265 ± 353	6.1 ± 0.7	8244 ± 912***	23.1 ± 1.7	17.0	3.64	yes
Q312R	c.935 A>G	6594 ± 696	18.5 ± 1.3	11214 ± 795***	31.9 ± 1.4	13.4	1.70	yes
D313G	c.938 A>G	9017 ± 723	25.5 ± 1.0	14089 ± 851***	40.4 ± 1.4	14.9	1.56	yes
D313Y	c.937 G>T	19526 ± 1460	59.0 ± 3.1	26474 ± 1225***	80.9 ± 2.4	21.8	1.36	yes
V316E	c.947 T>A	BLD	N/A	256 ± 26***	0.8 ± 0.1	0.8	NC	no
V316G	c.947 T>G	211 ± 17	0.7 ± 0.1	1151 ± 57***	3.8 ± 0.1	3.1	5.47	yes
V316I	c.946 G>A	27748 ± 1279	92.1 ± 3.6	37859 ± 1752***	126.1 ± 5.5	34.0	1.36	yes
I317N	c.950 T>A	BLD	N/A	967 ± 68***	2.9 ± 0.2	2.9	NC	no
I317S	c.950 T>G	BLD	N/A	243 ± 16***	0.8 ± 0	0.8	NC	no
I317T	c.950 T>C	2298 ± 338	6.5 ± 0.6	7812 ± 530***	23.6 ± 1.0	17.0	3.40	yes
I319F	c.955 A>T	781 ± 38	2.6 ± 0.1	5879 ± 252***	19.6 ± 0.7	17.0	7.53	yes
I319T	c.956 T>C	3462 ± 303	10.3 ± 0.6	9297 ± 626***	28.0 ± 1.2	17.7	2.69	yes
N320I	c.959 A>T	459 ± 44	1.4 ± 0.1	5660 ± 340***	17.1 ± 0.5	15.7	12.34	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
N320K	c.960 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
N320Y	c.958 A>T	BLD	N/A	188 ± 30***	0.6 ± 0.1	0.6	NC	no
Q321E	c.961 C>G	BLD	N/A	944 ± 61***	2.9 ± 0.1	2.9	NC	no
Q321H	c.963 G>C	620 ± 61	1.9 ± 0.1	6430 ± 466***	19.8 ± 0.9	17.9	10.38	yes
Q321H/D322N	c.963-964 GG>CA	BLD	N/A	BLD	N/A	N/A	N/A	no
Q321L	c.962 A>T	944 ± 78	2.9 ± 0.2	8091 ± 733***	24.6 ± 1.4	21.6	8.57	yes
Q321R	c.962 A>G	7398 ± 652	22.3 ± 1.3	21497 ± 1284***	66.1 ± 1.9	43.8	2.91	yes
D322E	c.966 C>A	2398 ± 141	6.7 ± 0.2	9554 ± 667***	26.8 ± 1.3	20.0	3.98	yes
D322N$^{\varphi}$	c.964 G>A	11843 ± 924	36.1 ± 1.8	15122 ± 976*	46.4 ± 1.6	10.3	1.28	yes
G325D	c.974 G>A	BLD	N/A	311 ± 26***	1.0 ± 0.1	1.0	NC	no
G325R	c.973G>C	909 ± 31	2.6 ± 0.1	9244 ± 417***	26.6 ± 1.4	24.0	10.17	yes
G325S	c.973 G>A	8102 ± 580	24.7 ± 1.1	20203 ± 1147***	62.5 ± 2.0	37.8	2.49	yes
Q327E	c.979 C>G	7436 ± 508	22.9 ± 1.1	16443 ± 1059***	50.4 ± 1.6	27.5	2.21	yes
Q327K	c.979 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G328A	c.983 G>C	2170 ± 69	6.9 ± 0.3	9054 ± 239***	28.7 ± 1.0	21.8	4.17	yes
G328E	c.983 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G328R	c.982 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G328V	c.983 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
G328W	c.982 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
Q333R$^{\varphi}$	c.998 A>G	28914 ± 1765	93.5 ± 2.5	34401 ± 1520*	113.1 ± 3.2	19.6	1.19	no
G334E	c.1001 G>A	26216 ± 1395	86.7 ± 3.4	31679 ± 1244**	105.5 ± 3.7	18.8	1.21	yes
E338K	c.1012 G>A	2179 ± 232	6.8 ± 0.4	5691 ± 331***	18.6 ± 0.8	11.8	2.61	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
V339E	c.1016 T>A	3805 ± 323	11.5 ± 0.6	6459 ± 488***	19.6 ± 0.6	8.1	1.70	yes
V339G	c.1016 T>G	BLD	N/A	471 ± 40***	1.5 ± 0.1	1.5	NC	no
W340R	c.1018 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
E341D	c.1023 A>C	BLD	N/A	519 ± 48***	1.6 ± 0.1	1.6	NC	no
E341K	c.1021 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
R342L	c.1025 G>T	BLD	N/A	BLD	N/A	N/A	N/A	no
R342P	c.1025 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
R342Q	c.1025 G>A	BLD	N/A	282 ± 23***	0.9 ± 0.1	0.9	NC	no
P343L	c.1028 C>T	11040 ± 397	36.6 ± 0.9	14919 ± 583***	49.6 ± 1.5	13.0	1.35	yes
L344P	c.1031 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
S345P	c.1033 T>C	BLD	N/A	1194 ± 92***	3.7 ± 0.2	3.7	NC	yes
A348P	c.1042 G>C	162 ± 24	0.5 ± 0.1	789 ± 73***	2.4 ± 0.2	1.9	4.88	no
W349R	c.1045 T>C	BLD	N/A	255 ± 31***	0.8 ± 0.1	0.8	NC	no
W349S	c.1046 G>C	5288 ± 337	16.5 ± 0.7	10035 ± 618***	31.4 ± 1.7	15.0	1.90	yes
A350P	c.1048 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A352D	c.1055 C>A	BLD	N/A	532 ± 46***	1.6 ± 0.1	1.6	NC	no
A352P	c.1054 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
A352V	c.1055 C>T	15153 ± 1083	44.5 ± 1.8	23791 ± 1662***	70.2 ± 3.2	25.7	1.57	yes
353insT, or 353ins1aa	c.1055_57 dup CTA ; or, c.1054_1055 ins CTA	BLD	N/A	BLD	N/A	N/A	N/A	no
I354K	c.1061 T>A	583 ± 66	1.7 ± 0.1	7398 ± 555***	21.6 ± 0.9	19.9	12.68	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
N355K	c.1065 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
R356G	c.1066 C>G	4702 ± 213	15.4 ± 0.7	11329 ± 719***	36.2 ± 1.2	20.8	2.41	yes
R356Q	c.1067G>A	12084 ± 634	36.1 ± 1.5	25098 ± 1433***	75.1 ± 3.6	39.0	2.08	yes
R356W	c.1066 C>T	3526 ± 240	11.0 ± 0.7	15570 ± 830***	49.1 ± 2.6	38.1	4.42	yes
Q357X	c.1069 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
358del1 or 358del or del358aa	c.1072 DelGAG	BLD	N/A	BLD	N/A	N/A	N/A	no
E358A	c.1073 A>C	625 ± 31	1.9 ± 0.1	5625 ± 385***	16.6 ± 0.8	14.7	8.99	yes
E358D	c.1074 G>T	2142 ± 84	6.3 ± 0.2	10553 ± 268***	31.0 ± 0.7	24.7	4.93	yes
E358G	c.1073 A>G	BLD	N/A	1967 ± 274***	5.5 ± 0.5	5.5	NC	yes
E358K	c.1072 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
I359T	c.1076 T>C	11337 ± 464	33.7 ± 1.7	21598 ± 466***	63.9 ± 2.0	30.3	1.91	yes
G360C	c.1078 G>T	2965 ± 152	8.7 ± 0.5	5668 ± 189***	16.8 ± 0.7	8.0	1.91	yes
G360D	c.1079 G>A	344 ± 23	1.0 ± 0.1	2457 ± 160***	7.2 ± 0.4	6.2	7.13	yes
G360S	c.1078 G>A	3350 ± 162	10.0 ± 0.6	7424 ± 188***	22.1 ± 0.9	12.1	2.22	yes
G361A	c.1082 G>C	2443 ± 73	7.2 ± 0.3	10112 ± 346***	30.0 ± 1.3	22.8	4.14	yes
G361E	c.1082 G>A	790 ± 21	2.6 ± 0.1	3894 ± 124***	13.4 ± 1	10.8	4.93	yes
G361R	c.1081 G>A	155 ± 15	0.5 ± 0.0	1004 ± 34***	3.0 ± 0.1	2.5	6.50	no
P362L	c.1085 C>T	947 ± 41	2.8 ± 0.1	6610 ± 196***	19.6 ± 0.8	16.8	6.98	yes
P362T	c.1084 C>A	9824 ± 630	32 ± 1.7	20927 ± 714***	70.5 ± 4.5	38.5	2.13	yes
R363C	c.1087 C>T	3994 ± 183	11.9 ± 0.6	12104 ± 379***	36.0 ± 1.6	24.1	3.03	yes
R363H	c.1088 G>A	7021 ± 382	20.0 ± 0.8	17613 ± 636***	50.5 ± 1.6	30.6	2.51	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
R363P	c.1088 G>C	BLD	N/A	269 ± 17***	0.8 ± 0.0	0.8	NC	no
A368T	c.1102 G>A	17725 ± 667	54.6 ± 1.7	23438 ± 471***	72.6 ± 1.8	18.0	1.32	yes
L372P	c.1115 T>C	388 ± 23	1.2 ± 0.1	848 ± 34***	2.6 ± 0.1	1.4	2.18	no
L372Q	c.1115 T>A	260 ± 23	0.8 ± 0.1	522 ± 37***	1.6 ± 0.1	0.8	2.01	no
L372R	c.1115 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
G373D	c.1118 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
G373R	c.1117 G>C	BLD	N/A	BLD	N/A	N/A	N/A	no
G373S	c.1117 G>A	1544 ± 69	4.8 ± 0.3	5128 ± 288***	15.7 ± 0.8	10.9	3.32	yes
G375_V376del	c.1124_1129del GAGTGG	807 ± 49	2.6 ± 0.2	1519 ± 69***	5 ± 0.3	2.4	1.88	no
A377D	c.1130 C>A	BLD	N/A	226 ± 20***	0.7 ± 0.1	0.7	NC	no
c.1129_1130 ins GCCTGTAATC CT, or ins377-4aa	c.1129 ins GCCTGTAATCC T; inserts after c.1128ntd	BLD	N/A	BLD	N/A	N/A	N/A	no
C378R	c.1132 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
C378Y	c.1133 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
382del-1aa or 382del1 or 382del	c.1145 DelCTT	BLD	N/A	BLD	N/A	N/A	N/A	no
C382W	c.1146 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
C382Y	c.1145 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
I384N	c.1151 T>A	BLD	N/A	283 ± 13***	0.8 ± 0.0	0.8	NC	no
T385A	c.1153 A>G	19434 ± 617	57.3 ± 2.1	24959 ± 770***	73.5 ± 2.4	16.1	1.28	yes

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
T385P	c.1153 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
Q386P	c.1157 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
P389A	c.1165 C>G	927 ± 33	2.7 ± 0.1	1348 ± 37***	4.0 ± 0.1	1.2	1.45	no
P389L	c.1166 C>T	BLD	N/A	188 ± 14**	0.6 ± 0	0.6	NC	no
P389R	c.1166 C>G	BLD	N/A	BLD	N/A	N/A	N/A	no
V390frX8	c.1168 Ins T	BLD	N/A	BLD	N/A	N/A	N/A	no
K391T	c.1172 A>C	9593 ± 351	30.1 ± 1.4	15199 ± 410***	47.4 ± 1.5	17.4	1.58	yes
G395A	c.1184 G>C	7664 ± 643	24.4 ± 1.3	9673 ± 668**	30.7 ± 1.0	6.3	1.26	yes
G395E	c.1184 G>A	3430 ± 248	11.9 ± 1.3	5489 ± 348***	19.7 ± 2.2	7.8	1.60	yes
c.1184insTAG, or ins395aa	c.1184 ins TAG; inserts after c.1183	572 ± 29	1.9 ± 0.1	911 ± 30***	3.1 ± 0.2	1.2	1.59	no
F396Y	c.1187 T>A	35640 ± 1129	111.2 ± 4.0	37319 ± 960	116.4 ± 3.3	5.1	1.05	no
E398K	c.1192 G>A	20150 ± 818	63.2 ± 3.2	36488 ± 824***	113.6 ± 2.6	50.4	1.81	yes
W399X	c.1196 G>A	BLD	N/A	BLD	N/A	N/A	N/A	no
401ins(T-S)	c.1202 Ins GACTTC	2075 ± 94	6.5 ± 0.4	4717 ± 230***	14.8 ± 0.8	8.3	2.27	yes
403del-1aa or 403del or 403del1	c.1208 DelAAG	BLD	N/A	BLD	N/A	N/A	N/A	no
L403S	c.1208 T>C	4480 ± 136	14.0 ± 0.5	6076 ± 133***	19.0 ± 0.5	4.9	1.36	yes
S405R	c.1213 A>C	15547 ± 652	52.5 ± 3.7	17297 ± 744*	59.6 ± 5.1	7.1	1.11	no
H406R$^{\varphi}$	c.1217 A>G	23858 ± 567	74.2 ± 1.6	23512 ± 589	73.2 ± 1.7	N/A	N/A	no
I407K	c.1220 T>A	BLD	N/A	BLD	N/A	N/A	N/A	no
I407R	c.1220 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
I407V$^{\varphi}$	c.1219 A>G	31074 ± 943	85.6 ± 2.8	35444 ± 671***	97.7 ± 2.3	12.1	1.14	no
P409A	c.1225 C>G	1111 ± 54	3.1 ± 0.2	10481 ± 445***	28.9 ± 1.3	25.9	9.43	yes
P409S	c.1225 C>T	883 ± 47	2.4 ± 0.1	8378 ± 315***	23.0 ± 0.8	20.6	9.49	yes
P409T	c.1225 C>A	986 ± 56	2.7 ± 0.2	8949 ± 558***	24.7 ± 1.6	22.0	9.07	yes
T410A	c.1228 A>G	380 ± 19	1.0 ± 0.1	4052 ± 135***	11.2 ± 0.4	10.1	10.65	yes
T410I	c.1229 C>T	146 ± 22	0.4 ± 0.1	4437 ± 274***	12.2 ± 0.8	11.8	30.37	yes
T410K	c.1229 C>A	BLD	N/A	BLD	N/A	N/A	N/A	no
T410P	c.1228 A>C	BLD	N/A	BLD	N/A	N/A	N/A	no
G411D	c.1232 G>A	409 ± 37	1.1 ± 0.1	3429 ± 148***	9.6 ± 0.4	8.5	8.38	yes
T412N	c.1235 C>A	360 ± 37	1.0 ± 0.1	5025 ± 255***	14.2 ± 0.8	13.2	13.95	yes
L414S	c.1241 T>C	BLD	N/A	403 ± 43***	1.2 ± 0.1	1.2	NC	no
L415F	c.1243 C>T	27736 ± 1380	91.8 ± 5.1	30643 ± 1340*	103.3 ± 7.2	11.6	1.10	no
L415P	c.1244 T>C	BLD	N/A	BLD	N/A	N/A	N/A	no
Q416X	c.1246 C>T	BLD	N/A	BLD	N/A	N/A	N/A	no
L417R	c.1250 T>G	BLD	N/A	BLD	N/A	N/A	N/A	no
E418G	c.1253 A>G	19226 ± 811	67.5 ± 1.7	25426 ± 910***	89.4 ± 1.5	21.9	1.32	yes
M421V	c.1261 A>G	25172 ± 1665	83.0 ± 3.4	32805 ± 2008**	108.6 ± 4.3	25.6	1.30	yes
X430Q, X430Qins30aa, or, X430QextX30	c.1288 T>C, c.1291 ins AATGTTTATTT TATTGCCAACT ACTACTTCCTG TCCACCTTTTTC TCCATTCACTT TAAAAGCTCAA	158 ± 13	0.5 ± 0.1	314 ± 28***	1.1 ± 0.1	0.5	1.99	no conclusion

α-Gal A Mutant Form		-Migalastat		+Migalastat		Absolute Increase at 10 µM (%WT)	α-Gal A Activity at 10 µM – Fold Over Baseline	Meets Amenable Mutation Criteria? (Yes/No)
Amino Acid Change	**Nucleotide Change**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**	**α-Gal A Activity (nmol/mg/hr)**	**% WT**			
	GGCTAGGTGGCTCATGCCTGTAA							

Data are expressed as the mean ± SEM of twenty data points: mutant α-Gal A activity expressed as a percent of the α-Gal A activity measured in wild-type cell lysates incubated without migalastat (-Migalastat) assayed in parallel.

"Absolute Increase at 10 µM (%WT)": the percent wild-type α-Gal A activity with 10 µM migalastat (+Migalastat) minus the baseline (-Migalastat) percent wild-type α-Gal A activity.

" α-Gal A Activity at 10 µM –Fold Over Baseline ": α-Gal A activity in mutant-transfected cell lysate with 10 µM migalastat / α-Gal A activity in mutant-transfected cell lysate without migalastat.

Statistically significant differences in α-Gal A activity without migalastat (n=20) versus with 10 µM migalastat (n=20) were determined using a one-tailed Mann-Whitney U non-parametric test: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. One or more asterisks indicate α-Gal A mutant forms that show a statistically significant increase in α-Gal A activity after incubation with 10 µM migalastat.

"BLD" indicates that the mean α-Gal A activity (mean of n=20) was below the limit of detection (<142 nmol/mg/hr; value is equal to 3 * standard deviation of the pcDNA activity in nmol/mg/hr after vector subtraction across 128 samples assayed in ten method validation experiments).

"Meets Amenable Mutation Criteria? (Yes/No)":

-"yes", if a mutant form shows a statistically significant increase in response to 10 µM migalastat and also meets the following criteria:

α-Gal A activity in the presence of 10 µM migalastat that is ≥1.20-fold over baseline[1] with an absolute increase of ≥3.0% of wild-type α-Gal A activity[2].

[1]The α-Gal A activity at 10 µM –fold over baseline is not calculated for mutant forms with a baseline α-Gal A activity that is BLD; for these mutant forms the criteria are met solely on the basis of the absolute increase criterion.

[2]For mutant forms with a baseline α-Gal A activity that is BLD, this criterion is met if the α-Gal A activity at 10 µM migalastat is ≥3.0% of wild-type.

-"no", if a mutant form is not qualified for testing in the GLP HEK assay, does not show a statistically significant increase in response to 10 µM migalastat, and/or does not meet the above criteria

-"no conclusion", if two independent lots of a specific plasmid failed the qPCR assay acceptance criteria after two consecutive transient transfection runs for each lot, but passed the GLP HEK assay acceptance criteria and the results for the α-Gal A mutant form did not meet the amenable mutation criteria.

N/A: Not Applicable. NC: not calculable. [φ]Mutation not yet reported as Fabry disease associated.

A listing of all Fabry disease mutations with literature phenotypes is provided in a separate Appendix.

Table 2S: Clinical Studies and Sources Used to Assess Clinical Validation of GLP HEK Assay by Parameter

Parameter	Gender(s) Included	Clinical Source(s)
α-Gal A	M	Lymphoblast: 74 cell lines PBMCs: Studies 201-203, 011, and 012
GL-3 inclusions per kidney interstitial capillary	M	Study 011
Lyso-Gb_3	M only M and F	Studies 011 and 012
Characteristics of amenable mutations from clinical studies compared to all amenable mutations identified in GLP HEK assay	M and F	Studies 201-204, 011, and 012

PBMCs: Peripheral blood mononuclear cells | M: males; F: females | α-Gal A: α-Galactosidase A | GL-3: Globotriaosylceramide | Lyso-Gb_3: Plasma globotriaosylsphingosine

Table 3S: Comparison of the Mutant α-Gal A Responses to Migalastat in the GLP HEK Assay and in PBMCs of Male Fabry Patients after Oral Administration of Migalastat in Phase 2

Meets Criteria	Patient	Protein change	Per Protocol Dose and Regimen	Phase 2 PBMC Assay (% Normal)								Phase 2 PBMC Response
				Baseline	+ Migalastat							
					Wk 2	Wk 4	Wk 6/8	Wk 12	Wk 24	Wk 36	Wk 48	
Yes	201-101	p.A143T	25,100,250 mg BID, 50 mg QD	23.6	66.4	60.5	64.1	79.1	70.5	87.3	90.0	Good
	201-102	p.T41I	25,100,250 mg BID, 50 mg QD	21.4	89.6	122.3	126.8	111.8	NA	110.5	112.3	Good
	201-103	p.T41I	25,100,250 mg BID, 50 mg QD	30.0	74.1	121.8	151.4	111.8	NA	136.8	118.2	Good
	201-104	p.A97V	25,100,250 mg BID, 50 mg QD	4.6	53.2	65.9	69.6	67.3	NA	62.7	42.7	Good
	201-105	p.A143T	25,100,250 mg BID, 50 mg QD	48.6	NA	NA	NA	72.3	NA	NA	NA	Good
	201-106	p.M51K	25,100,250 mg BID, 50 mg QD	4.1	23.6	30.0	20.5	17.7	15.9	17.7	28.2	Good
	201-204	p.G328A	25,100,250 mg BID, 50 mg QD	0.0	1.8	2.3	6.4	1.8	0.5	0.9	NA	Good
	201-305	p.L300P	25,100,250 mg BID, 50 mg QD	0.9	7.3	6.8	13.2	1.4	0.5	2.3	2.7	Good
	201-109	p.R301Q	150 mg QD (*in vivo* screen)	2.3	11.8	NA	NA	NA	NA	NA	NA	Good
	202-202	p.R301Q	150 mg QOD	1.4	NA	34.2	29.3	33.5	32.4	35.0	27.6	Good
	202-103	p.P259R	150 mg QOD	1.1	NA	10.1	8.0	10.5	NA	NA	1.6	Good
	202-104	p.P259R	150 mg QOD	1.0	NA	13.1	14.5	11.1	15.3	0.0	0.0	Good
	203-301	p.F295C	150 mg QOD	0.2	NA	0.5	NA	1.0	1.6	2.5	0.5	Good
	203-RF01	p.N215S	150 mg QOD	15.5	NA	38.5	55.0	48.2	49.6	50.9	33.6	Good
	203-RF03	p.P205T	150 mg QOD	0.8	NA	1.4	2.6	1.7	6.0	8.8	14.2	Good
No	201-107	p.G171D	150 mg QD (*in vivo* screen)	1.8	1.8	NA	NA	NA	NA	NA	NA	Non/Limited
	201-307	p.G271C	150 mg QD (*in vivo* screen)	27.3	0.5	NA	NA	NA	NA	NA	NA	Non/Limited
	201-401	p.R227Q	150 mg QD (*in vivo* screen)	0.5	0.5	NA	NA	NA	NA	NA	NA	Non/Limited
	201-501	p.H225R	150 mg QD (*in vivo* screen)	1.8	1.4	NA	NA	NA	NA	NA	NA	Non/Limited
	201-205	p.S276G	25,100,250 mg BID, 50 mg QD	0.5	4.1	7.7	5.5	4.1	3.6	4.6	NA	Good
	202-102	p.L415P	150 mg QOD	0.6	NA	0.6	0.0	0.0	0.8	NA	0.6	Non/Limited
	203-302	p.C94S	150 mg QOD	0.3	NA	0.4	0.3	NA	0.6	0.3	0.5	Non/Limited
	203-303	p.R112C	150 mg QOD	0.6	NA	NA	NA	NA	1.4	1.0	1.5	Non/Limited

‘Meets Criteria’ refers to the mutant α-Gal A responses to migalastat in the GLP HEK assay grouped according to the amenable mutation criteria. Then, these were compared to the PBMC α-Gal A responses of male Fabry patients with the corresponding *GLA* mutations who had been orally administered migalastat during Phase 2 clinical trials. Patients enrolled in FAB-CL-201 were orally administered migalastat at doses of 25 mg twice a day for the first two weeks, 100 mg twice a day during weeks 3 and 4, 250 mg twice a day during weeks 5 and 6, followed by 50 mg once per day during weeks 7 through 12. Separately, six other patients enrolled in FAB-CL-201, in the ‘Per Protocol Dose and Regimen’ section, were orally administered 150 mg migalastat every day for two weeks during a screening period and then tested for an *in vivo* PBMC α-Gal A response (this *in vivo* screen was conducted under a protocol amendment). Five of these six patients indicated by the phrase ‘(*in vivo* screen)’ are represented here; the sixth, had an insertion mutation which was not tested in the *in vitro* assay, and thus that patient is not represented in this table. None of these patients who met the other eligibility criteria (see ClinicalTrials.gov), responded with increased PBMC α-Gal A levels after migalastat administration, and thus did not participate in the remainder of the study. Patients enrolled in FAB-CL-202 and FAB-CL-203 were orally administered 150 mg migalastat every other day for the duration of the weeks indicated. In the PBMC assay, the baseline α-Gal A activity (-migalastat) presents the values from the last pre-dose sample. In the PBMC assay, the α-Gal A activity (+migalastat) presents the values after 150 mg (FAB-CL-202, FAB-CL-203, and FAB-CL-201 *in vivo* screen) or 25, 50, 100, or 250 mg (FAB-CL-201) migalastat administration at different regimens (‘QD’, ‘QOD’, and ‘BID’ refer to ‘every day’, ‘once every other day’ and ‘twice per day’) and time points (‘Wk’ refers to ‘week’) as specified in accordance with the different clinical protocols. In ‘Phase 2 PBMC Response’, patients were categorized according to their maximal net α-Gal A increase from baseline after treatment with migalastat. Patients with a 2% of normal or greater net increase were categorized as showing “good” responses, and patients with less than a 2% of normal net increase were categorized as showing “non/limited” responses. The mean normal α-Gal A activity in PBMCs from healthy volunteers was 22 nmol of free 4-MU released/mg protein/hr. ‘NA’ refers to ‘not available’ due to one or more of the following reasons: a) time point not part of the clinical study protocol, b) patient discontinued, c) sample not received, d) sample not analyzed due to poor sample quality.

Table 4S: Comparison of the Mutant α-Gal A Responses in the GLP HEK Assay and in PBMCs of Male Patients After Oral Administration of Migalastat in Study 011

GLP HEK Amenable?	Patient	Protein change	Stage 1-Stage 2 Treatment Category	Study 011 PBMC α-Gal A (% of Normal)			
					+ Migalastat		Study 011 PBMC Response
				Baseline[1]	6 Months[2]	12 Months[3]	
Yes	1101-005	p.G183D	Placebo-Migalastat	0	2.05	1.95	Good
	1101-007	p.L243F	Placebo-Migalastat	1.14	2.64	3.45	Good
	1601-003	p.I253T	Migalastat-Migalastat	2.86	17.68	33.55	Good
	1601-009	p.I253T	Migalastat-Migalastat	2.64	41.18	NA	Good
	1902-001	p.C174R	Migalastat-Migalastat	1.27	5.14	NA	Good
	2001-001	p.R356W	Placebo-Migalastat	1.68	49.86	48.23	Good
	2001-003	p.D55V/Q57L	Placebo-Migalastat	0.18	16.64	23.41	Good
	2001-005	p.G144V	Migalastat-Migalastat	0.23	0.36	0.73	Non/Limited
	2004-001	p.R301Q	Placebo-Migalastat	2.5	22.77	16.73	Good
	2016-901	p.G373S	Placebo-Migalastat	0.82	5.36	4.5	Good
	2026-906	p.D322E	Migalastat-Migalastat	0.91	7.09	5.91	Good
	2701-014	p.G325R	Migalastat-Migalastat	0.32	0.59	NA	Non/Limited
	3002-002	p.Y216C	Migalastat-Migalastat	0	6.77	2.45	Good
	4001-015	p.D33G	Placebo-Migalastat	4.09	39.95	43.95	Good
	5001-001	p.P259R	Placebo-Migalastat	3.27	13.27	10.55	Good
	5001-003	p.P259R	Placebo-Migalastat	3.14	11.64	12.86	Good
No	2004-901	p.R342Q	Placebo-Migalastat	0	0	0.32	Non/Limited
	2007-003	p.R342Q	Migalastat-Migalastat	0	0.23	0.27	Non/Limited
	2008-006	p.S276G	Migalastat-Migalastat	0.32	0.36	0.5	Non/Limited
	2015-001	p.R342Q	Placebo-Migalastat	0	0.18	NA	Non/Limited
	4001-010	p.S65I	Placebo-Migalastat	0.14	0.77	0.36	Non/Limited
	5003-008	p.R342Q	Migalastat-Migalastat	0.18	0.27	0	Non/Limited

'GLP HEK Amenable' refers to the mutant α-Gal A responses to migalastat in the GLP HEK cell-based assay grouped according to the "amenable" mutation criteria. These groups are aligned with the PBMC α-Gal A results from male patients with the corresponding α-Gal A mutant forms who had been orally administered migalastat at 150 mg every other day (QOD) during the Study 011 Phase 3 clinical trial.

PBMC α-Gal A is expressed as a percentage of normal (% of normal). The median normal α-Gal A activity in PBMCs from 16 non-Fabry patients was 22 nmol of free 4-MU released/mg protein/hr.

In 'Study 011 PBMC Response', patients were categorized according to their maximal net α-Gal A (% of normal) increase from baseline after 6 or 12 months of treatment with migalastat. Subjects with a 2% of normal or greater net increase after either duration of treatment were categorized as showing "good" responses, and patients with less than a 2% of normal net increase were categorized as showing "non/limited" responses.

The PBMC α-Gal A value at baseline was missing for one male patient (1601-006, D244N) treated with migalastat in Stage 1 and Stage 2. Therefore, this patient was excluded from this analysis and is not represented in this table.

The PBMC α-Gal A value at baseline from one male patient (4001-004, A156T) was implausible because it was higher than any baseline value from all other male patients in the study (in fact, the baseline value is within the typical range of baseline values from female patients in AT1001-011), and it was higher than any one of this male's other visits. Therefore, this patient was excluded from this analysis and is not represented in this table.

'NA' refers to 'not available' due to one or more of the following reasons: a) patient discontinued, b) sample not received, c) sample not analyzed due to poor sample quality.

[1]Baseline refers to the PBMC α-Gal A (% of normal) value at the Study 011 baseline visit (Visit 1) in patients treated with migalastat in Stage 1 and Stage 2; it refers to the PBMC α-Gal A (% of normal) value at month 6 in patients treated with placebo in Stage 1 and migalastat in Stage 2.

[2]6 months of migalastat refers to the PBMC α-Gal A (% of normal) value at month 6 in patients treated with migalastat in both Stage 1 and Stage 2; it refers to the PBMC α-Gal A (% of normal) value at month 12 in patients treated with placebo in Stage 1 and migalastat in Stage 2.

[3]12 months of migalastat refers to the PBMC α-Gal A (% of normal) value at month 12 in patients treated with migalastat in both Stage 1 and Stage 2; it refers to the PBMC α-Gal A (% of normal) value at month 18 (from the Open-Label Extension) in patients treated with placebo in Stage 1 and migalastat in Stage 2.

Table 5S: Comparison of the Mutant α-Gal A Responses in the GLP HEK Assay to Those in PBMCs of Male Patients After Oral Administration of Migalastat in Study 012

GLP HEK Amenable?	Patient	Protein change	Baseline to Month 18 Treatment Category	Study 012 PBMC α-Gal A (% of Normal)			
					+ Migalastat		Study AT1001-012 PBMC Response
				Baseline[1]	6 Months[2]	12 Months[3]	
Yes	1101-2401	p.R363H	Migalastat	15.23	79.55	56.0	Good
	1701-2651	p.A143T	Migalastat	45.18	71.09	100.68	Good
	2017-1451	p.P205T	Migalastat	4.09	8.09	7.59	Good
	2023-1765	p.N215S	Migalastat	9.05	44.27	36.32	Good
	2026-3101	p.D322E	Migalastat	2.64	5.55	6.0	Good
	2026-3103	p.D322E	Migalastat	3.32	5.45	2.82	Good
	2301-1154	p.N215S	Migalastat	10.14	44.36	43.64	Good
	2301-1156	p.N215S	Migalastat	10.95	62.59	51.41	Good
	2305-2301	p.N215S	Migalastat	9.55	49.23	45.77	Good
	2601-1101	p.A143T	Migalastat	50.91	83.95	112.27	Good
	4001-1053	p.M284T	Migalastat	0.73	2.77	2.23	Good
	4101-2451	p.Q312R	Migalastat	7.68	56.09	41.05	Good
	4102-2701	p.L403S	Migalastat	6.73	14.05	24.05	Good
	4104-2802	p.M96I	Migalastat	5.59	20.68	25.14	Good
No	5003-1851	p.R342Q	Migalastat	0.27	0.27	0.36	Non/Limited

'GLP HEK Amenable' refers to the mutant α-Gal A responses to migalastat in the GLP HEK cell-based assay grouped according to the "amenable" mutation criteria. These groups are aligned with the PBMC α-Gal A results from male patients with the corresponding α-Gal A mutant forms who had been orally administered migalastat HCl at 150 mg every other day (QOD) during the study AT1001-012 Phase 3 clinical trial.

PBMC α-Gal A is expressed as a percentage of normal (% of normal). The median normal α-Gal A activity in PBMCs from 16 non-Fabry patients was 22 nmol of free 4-MU released/mg protein/hr.

In 'Study AT1001-012 PBMC Response', patients were categorized according to their maximal net α-Gal A (% of normal) increase from baseline after 6 or 12 months of treatment with migalastat. Patients with a 2% of normal or greater net increase after either duration of treatment were categorized as showing "good" responses, and patients with less than a 2% of normal net increase were categorized as showing "non/limited" responses.

[1]Baseline refers to the PBMC α-Gal A (% of normal) value at the baseline visit in patients treated with migalastat.
[2]6 months of migalastat refers to the PBMC α-Gal A (% of normal) value at month 6 in patients treated with migalastat.
[3]12 months of migalastat refers to the PBMC α-Gal A (% of normal) value at month 12 in patients treated with migalastat.
The PBMC α-Gal A value at baseline was missing for one male subject (2301-1152, R342Q) treated with migalastat in Study AT1001-012. Therefore, this subject was excluded from this analysis and is not represented in this table.

Table 6S: Comparison of the Mutant α-Gal A Responses in the GLP HEK Assay to Those in PBMCs of Male Patients After Oral Administration of Migalastat (150 mg QOD) in Phase 2 and 3 Clinical Studies

	Subject	Protein change	Clinical Study	PBMC Response
Amenable	201-109	p.R301Q	FAB-201 (*in vivo* screen)	Good
	202-202	p.R301Q	FAB-202	Good
	202-103	p.P259R	FAB-202	Good
	202-104	p.P259R	FAB-202	Good
	203-301	p.F295C	FAB-203	Good
	203-RF01	p.N215S	FAB-203	Good
	203-RF03	p.P205T	FAB-203	Good
	1101-005	p.G183D	AT1001-011	Good
	1101-007	p.L243F	AT1001-011	Good
	1601-003	p.I253T	AT1001-011	Good
	1601-009	p.I253T	AT1001-011	Good
	1902-001	p.C174R	AT1001-011	Good
	2001-001	p.R356W	AT1001-011	Good
	2001-003	p.D55V/Q57L	AT1001-011	Good
	2001-005	p.G144V	AT1001-011	Non/Limited
	2004-001	p.R301Q	AT1001-011	Good
	2009-001	p.G373S	AT1001-011	Good
	2026-906	p.D322E	AT1001-011	Good
	2701-014	p.G325R	AT1001-011	Non/Limited
	3002-002	p.Y216C	AT1001-011	Good
	4001-015	p.D33G	AT1001-011	Good
	5001-001	p.P259R	AT1001-011	Good
	5001-003	p.P259R	AT1001-011	Good
	1101-2401	p.R363H	AT1001-012	Good
	1701-2651	p.A143T	AT1001-012	Good
	2017-1451	p.P205T	AT1001-012	Good
	2023-1765	p.N215S	AT1001-012	Good
	2026-3101	p.D322E	AT1001-012	Good
	2026-3103	p.D322E	AT1001-012	Good
	2301-1154	p.N215S	AT1001-012	Good
	2301-1156	p.N215S	AT1001-012	Good
	2305-2301	p.N215S	AT1001-012	Good

	2601-1101	**p.A143T**	**AT1001-012**	**Good**
	4001-1053	**p.M284T**	**AT1001-012**	**Good**
	4101-2451	**p.Q312R**	**AT1001-012**	**Good**
	4102-2701	**p.L403S**	**AT1001-012**	**Good**
	4104-2802	**p.M96I**	**AT1001-012**	**Good**
Non-Amenable	**201-107**	**p.G171D**	**FAB-201 (*in vivo* screen)**	**Non/Limited**
	201-307	**p.G271C**	**FAB-201 (*in vivo* screen)**	**Non/Limited**
	201-401	**p.R227Q**	**FAB-201 (*in vivo* screen)**	**Non/Limited**
	201-501	**p.H225R**	**FAB-201 (*in vivo* screen)**	**Non/Limited**
	202-102	**p.L415P**	**FAB-202**	**Non/Limited**
	203-302	**p.C94S**	**FAB-203**	**Non/Limited**
	203-303	**p.R112C**	**FAB-203**	**Non/Limited**
	2016-001	**p.R342Q**	**AT1001-011**	**Non/Limited**
	2007-003	**p.R342Q**	**AT1001-011**	**Non/Limited**
	2008-006	**p.S276G**	**AT1001-011**	**Non/Limited**
	2015-001	**p.R342Q**	**AT1001-011**	**Non/Limited**
	4001-010	**p.S65I**	**AT1001-011**	**Non/Limited**
	5003-008	**p.R342Q**	**AT1001-011**	**Non/Limited**
	5003-1851	**p.R342Q**	**AT1001-012**	**Non/Limited**

'GLP HEK Amenable' refers to the mutant α-Gal A responses to migalastat in the GLP HEK cell-based assay grouped according to the "amenable" mutation criteria. These groups are aligned with the PBMC α-Gal A results from male subjects with the corresponding α-Gal A mutant forms who had been orally administered migalastat at 150 mg every other day (QOD) during the Phase 2 and 3 clinical studies.

In 'PBMC Response', subjects were categorized according to their maximal net α-Gal A (% of normal) increase from baseline after treatment with migalastat. Subjects with a 2% of normal or greater net increase at any time after at least two weeks of treatment were categorized as showing "good" responses, and subjects with less than a 2% of normal net increase were categorized as showing "non/limited" responses.

Table 7S: Comparison between Mutant α–Gal A Responses in GLP HEK and Male Fabry Patient Kidney Interstitial Capillary GL-3 Responses in Study 011

GLP HEK Amenable?	Patient	Sex	Protein change	Stage 1-Stage 2 Treatment Category	Study 011 Male Patient Kidney IC GL-3	
					+ Migalastat	Study 011 Kidney IC GL-3 Response
					Absolute Change after 6 Months[1]	
Yes	1101-005	M	G183D	Placebo-Migalastat	-0.944	Good
	1101-007	M	L243F	Placebo-Migalastat	-1.134	Good
	2001-003	M	D55V/Q57L	Placebo-Migalastat	-0.093	Good
	2004-001	M	R301Q	Placebo-Migalastat	-0.053	Good
	4001-015	M	D33G	Placebo-Migalastat	-0.083	Good
	5001-001	M	P259R	Placebo-Migalastat	-2.281	Good
	1601-003	M	I253T	Migalastat-Migalastat	-0.083	Good
	1601-006	M	D244N	Migalastat-Migalastat	-1.125	Good
	2001-005	M	G144V	Migalastat-Migalastat	-1.775	Good
	2026-906	M	D322E	Migalastat-Migalastat	-1.102	Good
	3002-002	M	Y216C	Migalastat-Migalastat	-1.248	Good
	4001-004	M	A156T	Migalastat-Migalastat	-0.309	Good
No	2004-901	M	R342Q	Placebo-Migalastat	2.211	Non/Limited
	2015-001	M	R342Q	Placebo-Migalastat	1.271	Non/Limited
	4001-010	M	S65I	Placebo-Migalastat	0.982	Non/Limited
	2007-003	M	R342Q	Migalastat-Migalastat	0.851	Non/Limited
	2008-006	M	S276G	Migalastat-Migalastat	0.008	Non/Limited
	5003-008	M	R342Q	Migalastat-Migalastat	0.013	Non/Limited

'GLP HEK Amenable' refers to the mutant α-Gal A responses to migalastat in the GLP HEK cell-based assay grouped according to the "amenable" mutation criteria. These groups are aligned with the kidney IC GL-3 results from male (M) patients with the corresponding α-Gal A mutant forms who had been orally administered migalastat at 150 mg every other day (QOD) during Study 011.

[1]Each patient's kidney IC GL-3 absolute change after 6 months of treatment (i.e., baseline to month 6 for migalastat-migalastat; from month 6 to month 12 for placebo-migalastat) is provided.

In 'Study 011 Kidney IC GL-3 Response', patients with a kidney IC GL-3 absolute change <0.0 after 6 months of treatment were categorized as showing "good" responses, and patients with ≥0.0 were categorized as showing "non/limited" responses.

This analysis includes only male patients with baseline values ≥0.1.

Table 8S: Comparison Between Mutant α–Gal A Responses in GLP HEK and Male and Female Fabry Patient Plasma Lyso-Gb_3 Responses in Study 011

GLP HEK Amenable?	Patient	Sex	Protein change	Stage 1-Stage 2 Treatment Category	Study 011 Patient Plasma Lyso-Gb_3	
					+ Migalastat	Study 011 Plasma Lyso-Gb_3 Response
					Absolute Change after 6 Months[1]	
Yes	1101-007	M	L243F	Placebo-Migalastat	-61.1	Good
	2001-001	M	R356W	Placebo-Migalastat	-2.72	Good
	2001-003	M	D55V/Q57L	Placebo-Migalastat	-43.2	Good
	4001-015	M	D33G	Placebo-Migalastat	-25.6	Good
	5001-001	M	P259R	Placebo-Migalastat	-51.8	Good
	5001-003	M	P259R	Placebo-Migalastat	-1.97	Good
	1601-007	F	I253T	Placebo-Migalastat	-8.49	Good
	2701-012	F	G325R	Placebo-Migalastat	-0.7	Good
	3002-004	F	D264Y	Placebo-Migalastat	-0.3	Good
	4001-003	F	R301Q	Placebo-Migalastat	-0.27	Good
	4002-001	F	P205T	Placebo-Migalastat	-1.02	Good
	4002-005	F	G260A	Placebo-Migalastat	-3.3	Good
	9001-003	F	G85D	Placebo-Migalastat	-0.93	Good
	1601-006	M	D244N	Migalastat-Migalastat	-23.7	Good
	2001-005	M	G144V	Migalastat-Migalastat	-15.0	Good
	2026-906	M	D322E	Migalastat-Migalastat	-54.1	Good
	3002-002	M	Y216C	Migalastat-Migalastat	-24.0	Good
	4001-004	M	A156T	Migalastat-Migalastat	-69.7	Good
	1601-008	F	I253T	Migalastat-Migalastat	-2.19	Good
	2001-904	F	Y216C	Migalastat-Migalastat	-3.53	Good
	2006-001	F	R112H	Migalastat-Migalastat	0.17	Non/Limited
	2026-904	F	D322E	Migalastat-Migalastat	-2.37	Good
	2102-004	F	I270T	Migalastat-Migalastat	-1.01	Good
	2302-003	F	P259R	Migalastat-Migalastat	-2.37	Good
	3002-003	F	Y216C	Migalastat-Migalastat	-4.43	Good
	4001-016	F	P205T	Migalastat-Migalastat	-2.47	Good
	4002-004	F	M187I	Migalastat-Migalastat	0.16	Non/Limited
	6001-001	F	P293T	Migalastat-Migalastat	0.1	Non/Limited
	6001-002	F	P293T	Migalastat-Migalastat	1.23	Non/Limited
	9001-001	F	G271S, D313Y	Migalastat-Migalastat	-0.67	Good
	9001-004	F	A156T	Migalastat-Migalastat	1.8	Non/Limited
No	2004-901	M	R342Q	Placebo-Migalastat	9.33	Non/Limited
	4001-010	M	S65I	Placebo-Migalastat	5.67	Non/Limited

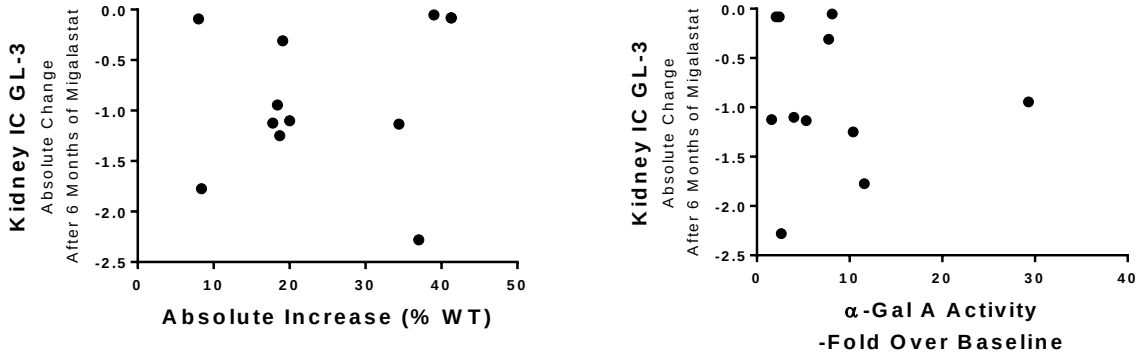
GLP HEK Amenable?	Patient	Sex	Protein change	Stage 1-Stage 2 Treatment Category	Study 011 Patient Plasma Lyso-Gb_3	
					+ Migalastat	Study 011 Plasma Lyso-Gb_3 Response
					Absolute Change after 6 Months[1]	
	2005-001	F	G261D	Placebo-Migalastat	15.2	Non/Limited
	2015-002	F	R342Q	Placebo-Migalastat	2.33	Non/Limited
	4001-014	F	I117S	Placebo-Migalastat	-1.23	Good
	5003-007	F	R342Q	Placebo-Migalastat	1.31	Non/Limited
	6001-005	F	L414S	Placebo-Migalastat	1.97	Non/Limited
	2007-003	M	R342Q	Migalastat-Migalastat	65.0	Non/Limited
	2008-006	M	S276G	Migalastat-Migalastat	2	Non/Limited
	5003-008	M	R342Q	Migalastat-Migalastat	29.7	Non/Limited
	2008-005	F	E48K	Migalastat-Migalastat	-8.57	Good
	2017-001	F	R49P	Migalastat-Migalastat	2.83	Non/Limited
	2101-001	F	G183V	Migalastat-Migalastat	1.93	Non/Limited

'GLP HEK Amenable' refers to the mutant α-Gal A responses to migalastat in the GLP HEK cell-based assay grouped according to the "amenable" mutation criteria. These groups are aligned with the plasma lyso-Gb_3 results from male and female patients with the corresponding α-Gal A mutant forms who had been orally administered migalastat at 150 mg every other day (QOD) during Study 011.

[1]Each patients' plasma lyso-Gb_3 absolute change after 6 months of treatment (i.e., baseline to month 6 for migalastat-migalastat; from month 6 to month 12 for placebo-migalastat) is provided.

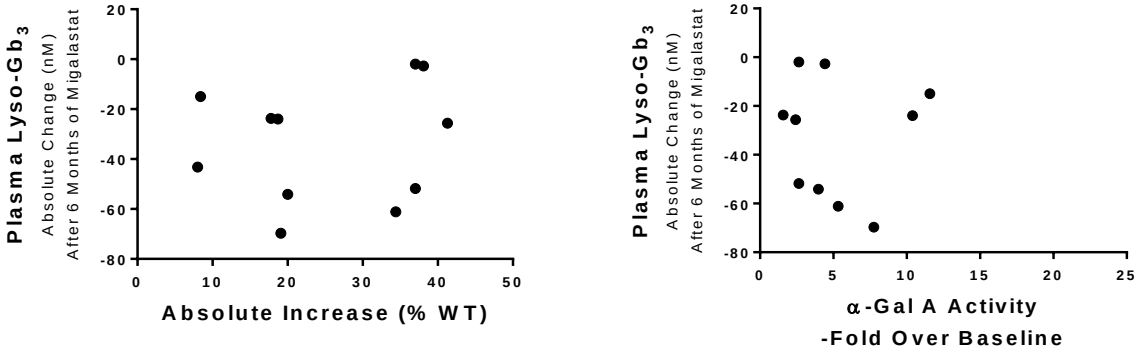
In 'Study 011 Plasma Lyso-Gb_3 Response', patients with a plasma lyso-Gb_3 absolute change <0.0 after 6 months of treatment were categorized as showing "good" responses, and patients with ≥0.0 were categorized as showing "non/limited" responses.

Figure 3S: Relationship of the Magnitude of Increase in α-Gal A Activity in the GLP HEK Assay with the Magnitude of Kidney Interstitial Capillary GL-3 Reduction in Male Patients in Study 011



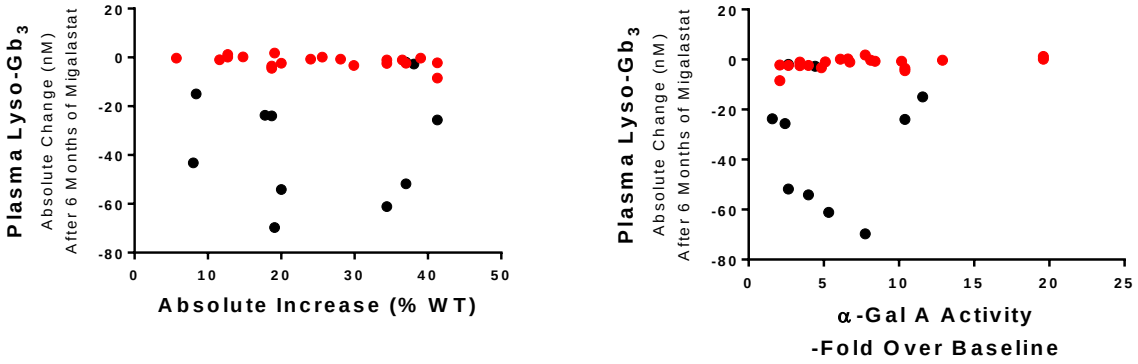
Left: Correlation analysis of the absolute increase of GLP HEK amenable mutant forms compared with the absolute change in kidney GL-3 inclusions after six months of migalastat in male patients in study 011. The Pearson correlation coefficient [*r*] was 0.2172 [n=12] (*p*=0.4978) (two-tailed p-value). **Right**: Correlation analysis of the α-Gal A activity –fold over baseline of GLP HEK amenable mutant forms compared with the absolute change in kidney GL-3 inclusions after six months of migalastat in male patients in study 011. The Pearson correlation coefficient [*r*] was -0.0712 [n=11] (*p*=0.8353) (two-tailed p-value). The α-Gal A activity –fold over baseline was not calculated for 1 mutant form with baseline activity that was below the limit of detection in the GLP HEK assay.

Figure 4S: Relationship of the Magnitude of Increase in α-Gal A Activity in the GLP HEK Assay with the Magnitude of Plasma Lyso-Gb_3 Reduction in Male Patients in Study 011



Left: Correlation analysis of the absolute increase of GLP HEK amenable mutant forms compared with the absolute change in plasma lyso-Gb_3 after six months of migalastat in male patients in study 011. The Pearson correlation coefficient [*r*] was 0.1653 [n=11] (p=0.6272) (two-tailed p-value). **Right**: Correlation analysis of the α-Gal A activity –fold over baseline of GLP HEK amenable mutant forms compared with the absolute change in plasma lyso-Gb_3 after six months of migalastat in male patients in study 011. The Pearson correlation coefficient [*r*] was -0.0248 [n=10] (*p*=0.9458) (two-tailed p-value). The α-Gal A activity –fold over baseline was not calculated for 1 mutant form with baseline activity that was below the limit of detection in the GLP HEK assay.

Figure 5S: Relationship of the Magnitude of Increase in α-Gal A Activity in the GLP HEK Assay with the Magnitude of Plasma Lyso-Gb_3 Reduction in Male and Female Patients in Study 011



Left: Correlation analysis of the absolute increase of GLP HEK amenable mutant forms compared with the absolute change in plasma lyso-Gb_3 after six months of migalastat in male (black dots) and female (red dots) patients in study 011. The Pearson correlation coefficient [*r*] was 0.0328 [n=31] (p=0.8608) (two-tailed p-value). **Right**: Correlation analysis of the α-Gal A activity –fold over baseline of GLP HEK amenable mutant forms compared with the absolute change in plasma lyso-Gb_3 after six months of migalastat in male (black dots) and female (red dots) patients in study 011. The Pearson correlation coefficient [*r*] was 0.2130 [n=30] (p=0.2584) (two-tailed p-value). The α-Gal A activity -fold over baseline was not calculated for 1 mutant form with baseline activity that was below the limit of detection in the GLP HEK assay.

Table 9S: Unique Amenable Mutations Represented in Phase 2 and 3 Studies

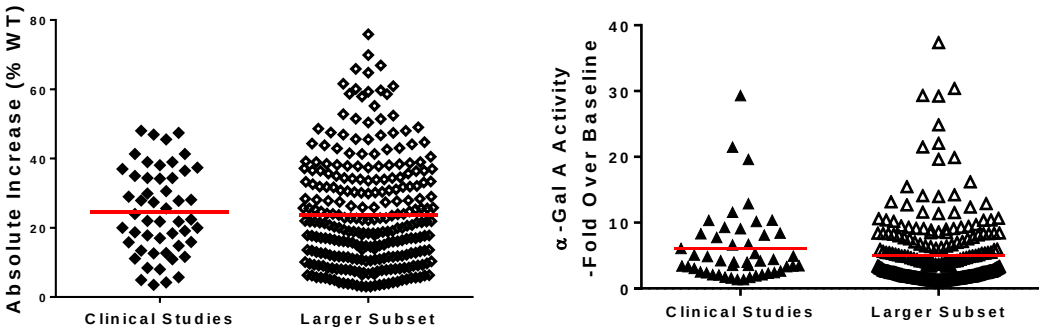
Unique Amenable Mutations	Clinical Study (# patients)
L32P	204 (1), 012 (3)
D33G	011 (1)
G35R	012 (1)
L36W	011 (2)
T41I	201 (2)
M51K	201 (1)
D55V/Q57L	011 (1), 012 (1)
G85D	011 (1), 012 (7)
M96I	012 (1)
A97V	201 (1), 012 (1)
R112G	012 (1)
R112H	204 (1), 011 (1), 012 (1)
A143T	201 (2), 012 (3)
G144V	011 (1)
A156T	011 (3), 012 (6)
C174R	011 (1)
G183D	011 (2)
M187I	011 (1)
P205T	203 (1), 204 (1), 011 (2), 012 (1)
N215S	203 (1), 012 (10)
Y216C	011 (3), 012 (1)
L243F	011 (1)
D244N	011 (1)
I253S	012 (1)
I253T	011 (4)
G258R	011 (2)
P259R	202 (2), 204 (2), 011 (3)
G260A	011 (1), 012 (1)
D264Y	011 (1)
I270T	011 (1)

Unique Amenable Mutations	Clinical Study (# patients)
G271S	011 (0.5)*
Q279E	012 (1)
M284T	011 (2), 012 (1)
P293T	011 (2)
F295C	203 (1), 011 (1)
M296I	012 (1)
L300P	201 (1), 011 (1)
R301P	012 (3)
R301Q	201 (1), 202 (1), 011 (3), 012 (1)
Q312R	012 (1)
D313Y	011 (0.5)*
I317T	011 (1)
D322E	011 (2), 012 (4)
G325R	011 (2)
G328A	201 (1), 012 (1)
R356Q	012 (1)
R356W	011 (1)
R363H	012 (1)
G373S	011 (1)
L403S	012 (1)
P409T	012 (1)
*indicates that G271S and D313Y were represented on two separate alleles in a female patient.	

Table 10S: Unique Non-amenable Mutations Represented in Phase 2 and 3 Studies

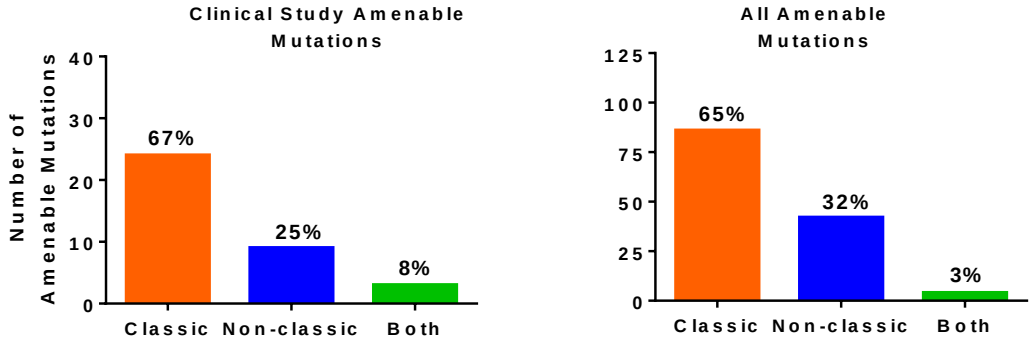
Unique Non-amenable Mutations	Clinical Study (# patients)
M1I	204 (1)
E48K	011 (1)
R49P	011 (1)
C52G	204 (1)
S65I[#]	011 (2)
C94S	203 (1)
R112C	203 (1)
I117S	011 (1)
G171D	201 (1)
G183V	011 (1)
H225R	201 (1)
R227Q	201 (1)
R227X[#]	204 (1)
G261D	011 (1)
G271C	201 (1)
S276G	201 (1), 011 (1)
E341D	012 (1)
R342Q	011 (8), 012 (3)
E358K	204 (1)
L414S	011 (1)
L415P	202 (1)
82InsG[#]	201 (1)
[#]S65I (putative splice site mutation based on change to the same nucleotide as reported in Lai et al, 2003), R227X (large truncation nonsense mutation), and 82InsG (frameshift mutation) did not qualify for testing in GLP HEK and are categorized as non-amenable.	

Figure 6S: Absolute Increase and α-Gal A Activity –Fold Over Baseline of Phase 2 and 3 Clinical Study Amenable Mutant Forms Compared to the Larger Subset That Met the Amenable Mutation Criteria



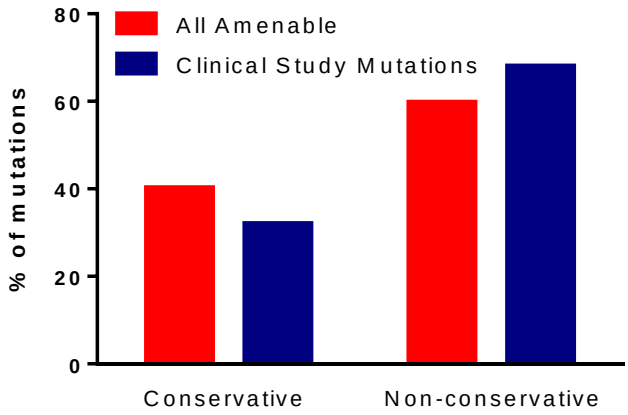
Each horizontal line indicates the mean of the absolute increase or α-Gal A activity –fold over baseline in response to migalastat. The mean ± SEM absolute increases for the clinical study cohort and larger subset were 24.7±1.7 (95% confidence intervals, 21.2, 28.2; n=51) and 23.7±0.9 (95% confidence intervals, 21.8, 25.6; n=268), respectively. The mean ± SEM α-Gal A activity –fold over baseline for the clinical study cohort and larger subset were 6.1±0.8 (95% confidence intervals, 4.5, 7.7; n=48) and 4.9±0.3 (95% confidence intervals, 4.3, 5.6; n=252), respectively. The α-Gal A activity –fold over baseline was not calculated for 16 mutant forms with baseline activity that was below the limit of detection in the GLP HEK assay.

Figure 7S: Amenable Mutations Grouped by Phenotype: Results for Phase 2 and 3 Clinical Studies Compared to the Larger Subset That Met the Amenable Mutation Criteria



Each bar represents the number of amenable mutations in each phenotype category; percentages (%) indicate the % of total amenable mutations with phenotype categories (n = 36 total for "Clinical Study Amenable Mutations"; n = 132 total for "All Amenable Mutations"); amenable mutations with unknown phenotype were excluded. "Both" = Amenable mutations associated with both classic and non-classic phenotypes.

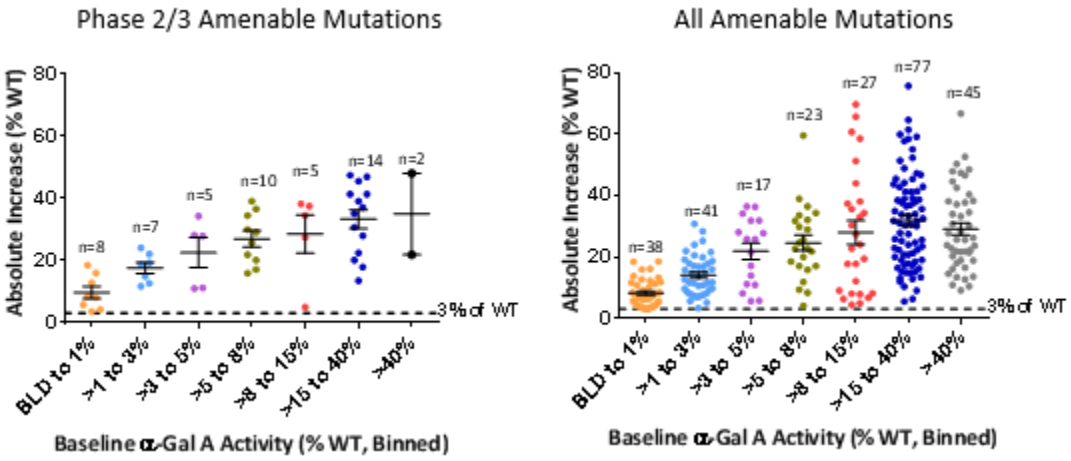
Figure 8S: Proportions of Conservative and Non-conservative Amino Acid Substitutions



The proportion of conservative and non-conservative amino acid substitutions of the amenable α-Gal A mutant forms in the clinical studies and the larger amenable subset are shown. The classification of "conservative" was made if the mutation resulted in the substitution of an amino acid with the same charge as the original residue, or with a similar hydrogen-bonding capacity. The classification of "non-conservative" was made if the mutation resulted in a substitution that changed the charge or the hydrogen-bonding capacity to a large degree. Six amenable complex missense mutations, small deletions, and small insertions were excluded from this analysis.

Figure 9S:

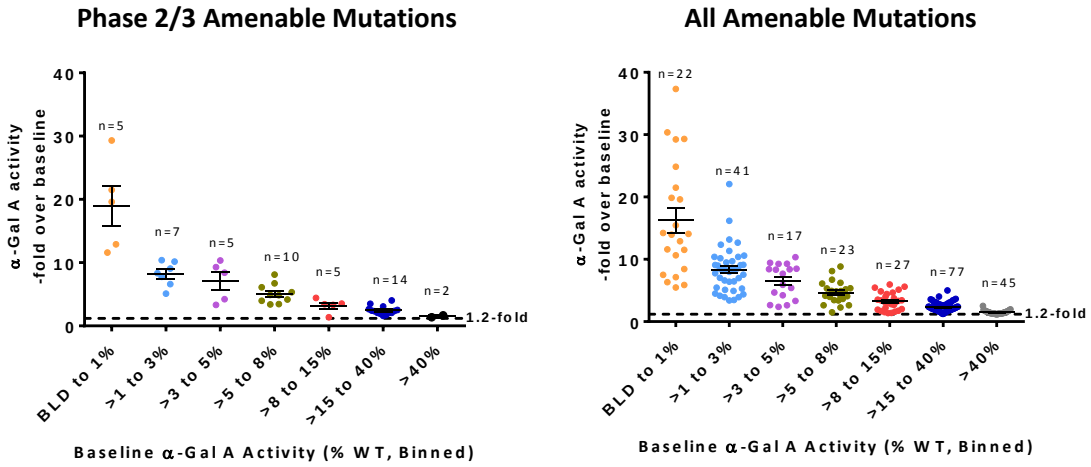
Absolute Increase in α-Gal A Activity as a Function of Baseline



The GLP HEK assay baseline α–Gal A activity of amenable mutant forms in clinical studies and of the larger subset was binned into categories of percentage of wild-type activity as indicated in the X-axis. The absolute increase in α-Gal A activity in response to 10 μM migalastat in the GLP HEK assay for the clinical study mutant forms and the larger subset are plotted on the Y-axis. Horizontal lines indicate the mean ± SEM. 'n' indicates the number of mutant forms in each category.

Figure 10S:

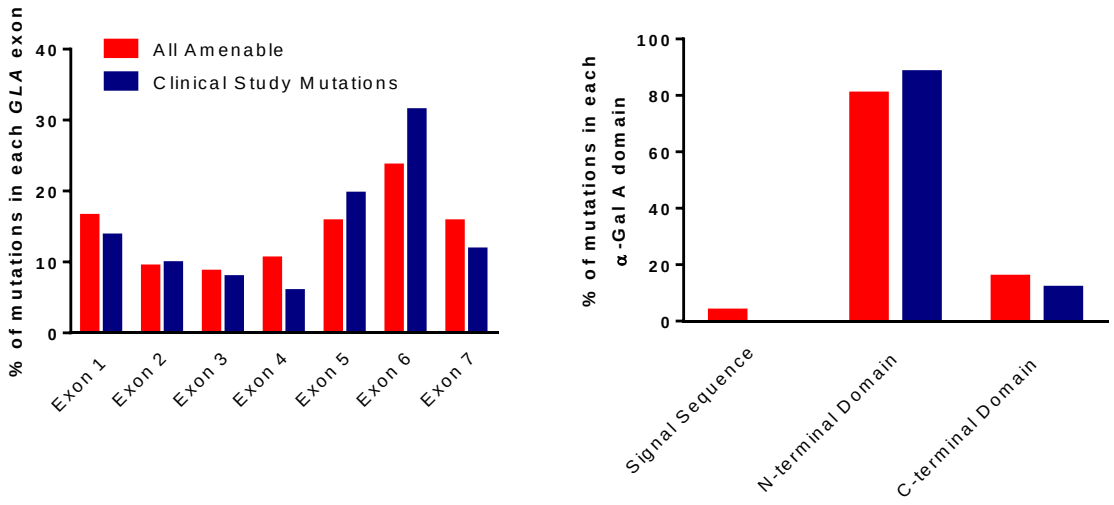
α-Gal A Activity –Fold Over Baseline as a Function of Baseline



The GLP HEK assay baseline α–Gal A activity of amenable mutant forms in clinical studies and of the larger subset was binned into categories of percentage of wild type activity as indicated in the X-axis. The α-Gal A activity –fold over baseline in response to 10 μM migalastat in the GLP HEK assay for the clinical study mutant forms and the larger subset are plotted on the Y-axis. Horizontal lines indicate the mean ± SEM. 'n' indicates the number of mutant forms in each category. Three and 16 amenable mutations in clinical studies and in the larger subset with baseline α-Gal A activity that was BLD, respectively, are excluded as the α-Gal A activity –fold over baseline was not calculable.

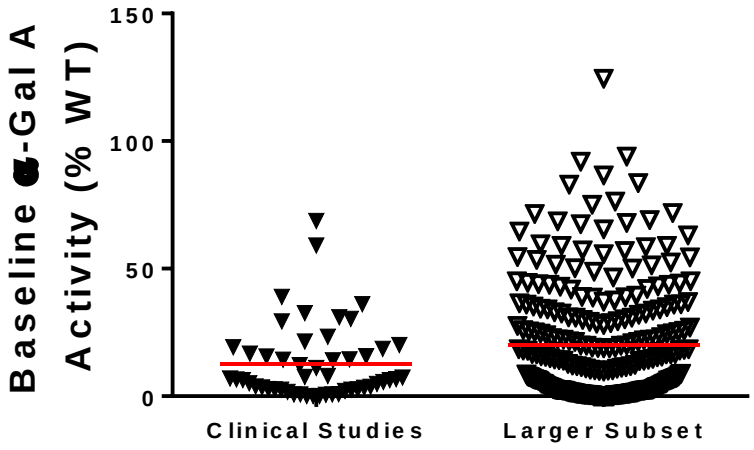
Figure 11S:

Locations of Substituted Amino Acid Residues in the GLA Gene and α-Gal A Protein



The *GLA* gene and α-Gal A protein structural distributions of the amenable mutations in the clinical studies and the larger amenable subset are shown. The left panel illustrates the structural distributions at the level of the *GLA* gene, and the right panel illustrates the structural distributions at the level of the protein. The junctions for each of the 7 exons translated to amino acid residues are as follows: amino acid residues 1-64, 65-123, 124-182, 183-213, 214-267, 268-333, and 334-429 for exons 1, 2, 3, 4, 5, 6, and 7, respectively. The amino acid residue junctions for each of the 3 structural domains are as follows: 1-31, 32-330, and 331-429 for the signal sequence, the N-terminal $(\beta/\alpha)_8$-barrel structural domain, and the C-terminal anti-parallel β-sheet domain. One amenable complex missense mutation that affected more than one exon (N215S/D313Y) was excluded from the analysis in the left panel.

Figure 12S: Mean baseline α-Gal A activity



Each horizontal line indicates the mean baseline activity (expressed as a percentage of wild-type; % WT) of the amenable α-Gal A mutant forms in the GLP HEK assay. The mean ± SEM baseline activity for the clinical study cohort and larger subset of amenable mutant forms were 12.7±2.1 (n=51) and 20.0±1.4 (n=268), respectively. Values that were below the limit of detection were imputed to zero (0) for this analysis.

Table 11SA:

The Pharmacogenetic Reference Table Based on the GLP HEK Assay Results

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.8 T>C	c.T8C	L3P
c.37 G>A	c.G37A	A13T
c.37 G>C	c.G37C	A13P
c.43 G>A	c.G43A	A15T
c.44 C>G	c.C44G	A15G
c.58 G>C	c.G58C	A20P
c.59 C>A	c.C59A	A20D
c.70 T>C	c.T70C	W24R
c.70 T>G	c.T70G	W24G
c.72 G>C	c.G72C	W24C
c.95 T>C	c.T95C	L32P
c.97 G>T	c.G97T	D33Y
c.98 A>G	c.A98G	D33G
c.101 A>G	c.A101G	N34S
c.102 T>G	c.T102G	N34K
c.103 G>C	c.G103C	G35R
c.107 T>C	c.T107C	L36S
c.107 T>G	c.T107G	L36W
c.108 G>C	c.G108C	L36F
c.109 G>A	c.G109A	A37T
c.110 C>T	c.C110T	A37V
c.122 C>T	c.C122T	T41I
c.124 A>C	c.A124C	M42L
c.124 A>G	c.A124G	M42V
c.125 T>A	c.T125A	M42K
c.125 T>C	c.T125C	M42T
c.125 T>G	c.T125G	M42R
c.137 A>C	c.A137C	H46P
c.142 G>C	c.G142C	E48Q
c.152 T>A	c.T152A	M51K

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.153 G>A	c.G153A	M51I
c.157 A>G	c.A157G	N53D
c.[157 A>C; 158 A>T]	c. A157C/A158T	N53L
c.160 C>T	c.C160T	L54F
c.161 T>C	c.T161C	L54P
c.164 A>T	c.A164T	D55V
c.[164 A>T; 170 A>T]	c.A164T/A170T	D55V/Q57L
c.167 G>T	c.G167T	C56F
c.167 G>A	c.G167A	C56Y
c.170 A>T	c.A170T	Q57L
c.175 G>A	c.G175A	E59K
c.178 C>A	c.C178A	P60T
c.178 C>T	c.C178T	P60S
c.179 C>T	c.C179T	P60L
c.196 G>A	c.G196A	E66K
c.197 A>G	c.A197G	E66G
c.214 A>G	c.A214G	M72V
c.216 G>A	c.G216A	M72I
c.218 C>T	c.C218T	A73V
c.227 T>C	c.T227C	M76T
c.247 G>A	c.G247A	D83N
c.253 G>A	c.G253A	G85S
c.254 G>A	c.G254A	G85D
c.[253 G>A; 254 G>T; 255 T>G]	c. G253A/G254T/T255G	G85M
c.265 C>T	c.C265T	L89F
c.272 T>C	c.T272C	I91T
c.288 G>A	c.G288A	M96I
c.289 G>C	c.G289C	A97P
c.290 C>T	c.C290T	A97V
c.305 C>T	c.C305T	S102L
c.311G>T	c.G311T	G104V
c.322 G>A	c.G322A	A108T

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.326 A>G	c.A326G	D109G
c.334 C>G	c.C334G	R112G
c.335 G>A	c.G335A	R112H
c.337 T>C	c.T337C	F113L
c.352 C>T	c.C352T	R118C
c.361 G>A	c.G361A	A121T
c.368 A>G	c.A368G	Y123C
c. 374 A>T	c.A374T	H125L
c.376 A>G	c.A376G	S126G
c.383 G>A	c.G383A	G128E
c.404 C>T	c.C404T	A135V
c.408 T>A	c.T408A	D136E
c.416 A>G	c.A416G	N139S
c.419 A>C	c.A419C	K140T
c.427 G>A	c.G427A	A143T
c.431 G>A	c.G431A	G144D
c.431 G>T	c.G431T	G144V
c.436 C>T	c.C436T	P146S
c.455 A>G	c.A455G	Y152C
c.466 G>A	c.G466A	A156T
c.467 C>T	c.C467T	A156V
c.484 T>G	c.T484G	W162G
c.493 G>C	c.G493C	D165H
c.494 A>G	c.A494G	D165G
c.[496 C>G; 497 T>G]	c. C496G/T497G	L166G
c.496 C>G	c.C496G	L166V
c.506 T>C	c.T506C	F169S
c.520 T>C	c.T520C	C174R
c.520 T>G	c.T520G	C174G
c.525 C>G	c.C525G	D175E
c.548 G>C	c.G548C	G183A
c.548 G>A	c.G548A	G183D

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.550 T>A	c.T550A	Y184N
c.551A>G	c.A551G	Y184C
c.553 A>G	c.A553G	K185E
c.559 A>G	c.A559G	M187V
c.560 T>C	c.T560C	M187T
c.561 G>T	c.G561T	M187I
c.559_564 dup	c.559_564dup	p. M187_S188 dup
c.572 T>A	c.T572A	L191Q
c.581 C>T	c.C581T	T194I
c.584 G>T	c.G584T	G195V
c.593 T>C	c.T593C	I198T
c.595 G>A	c.G595A	V199M
c.596 T>G	c.T596G	V199G
c.599 A>G	c.A599G	Y200C
c.602 C>T	c.C602T	S201F
c.602 C>A	c.C602A	S201Y
c.608 A>T	c.A608T	E203V
c.609 G>C	c.G609C	E203D
c.613 C>A	c.C613A	P205T
c.613 C>T	c.C613T	P205S
c.614 C>T	c.C614T	P205L
c.619 T>C	c.T619C	Y207H
c.620 A>C	c.A620C	Y207S
c.628 C>T	c.C628T	P210S
c.629 C>T	c.C629T	P210L
c.638 A>T	c.A638T	K213M
c.640 C>T	c.C640T	P214S
c.641 C>T	c.641T	P214L
c.643 A>G	c.A643G	N215D
c.644 A>G	c.A644G	N215S
c.[644 A>G; 937 G>T]	c. A644G/G937T	N215S/D313Y
c.646 T>G	c.T646G	Y216D

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.647 A>G	c.A647G	Y216C
c.656 T>A	c.T656A	I219N
c.656 T>C	c.T656C	I219T
c.659 G>A	c.G659A	R220Q
c.659 G>C	c.G659C	R220P
c.671 A>G	c.A671G	N224S
c.673 C>G	c.C673G	H225D
c.683 A>G	c.A683G	N228S
c.687 T>A	c.T687A	F229L
c.695 T>C	c.T695C	I232T
c.713 G>A	c.G713A	S238N
c.716 T>C	c.T716C	I239T
c.724 A>T	c.A724T	I242F
c.725 T>A	c.T725A	I242N
c.729 G>C	c.G729C	L243F
c.728 T>G	c.T728G	L243W
c.730 G>A	c.G730A	D244N
c.730 G>C	c.G730C	D244H
c.735 T>G	c.T735G	W245G
c.740 C>G	c.C740G	S247C
c.747 C>G	c.C747G	N249K
c.749 A>C	c.A749C	Q250P
c.758 T>C	c.T758C	I253T
c.758 T>G	c.T758G	I253S
c.760-762del GTT	c.760_762delGTT	p.V254del
c.769 G>C	c.G769C	A257P
c.770 C>G	c.C770G	A257G
c.772 G>C	c.G772C	G258R
c.773 G>T	c.G773T	G258V
c.776 C>G	c.C776G	P259R
c.776 C>T	c.C776T	P259L
c.779 G>A	c.G779A	G260E

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.779 G>C	c.G779C	G260A
c.788 A>G	c.A788G	N263S
c.790 G>T	c.G790T	D264Y
c.794 C>T	c.C794T	P265L
c.800 T>C	c.T800C	M267T
c.805 G>A	c.G805A	V269M
c.806 T>C	c.T806C	V269A
c.809 T>C	c.T809C	I270T
c.811 G>A	c.G811A	G271S
c.[811 G>A; 937 G>T]	c. G811A/G937T	G271S/D313Y
c.812 G>A	c. G812A	G271D
c.827 G>A	c.G827A	S276N
c.829 T>G	c.T829G	W277G
c.831 G>T	c.G831T	W277C
c.835 C>G	c.C835G	Q279E
c.838 C>A	c.C838A	Q280K
c.840 A>T	c.A840T	Q280H
c.844 A>G	c.A844G	T282A
c.845 C>T	c.C845T	T282I
c.850 A>G	c.A850G	M284V
c.851 T>C	c.T851C	M284T
c.862 G>C	c.G862C	A288P
c.866 T>G	c.T866G	I289S
c.868 A>C	c.A868C	M290L
c.870 G>A	c.G870A	M290I
c.871 G>A	c.G871A	A291T
c.877 C>A	c.C877A	P293T
c.881 T>C	c.T881C	L294S
c.884 T>G	c.T884G	F295C
c.886 A>G	c.A886G	M296V
c.886 A>T	c.A886T	M296L
c.887 T>C	c.T887C	M296T

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.888 G>A	c.G888A	M296I
c.893 A>G	c.A893G	N298S
c.897 C>G	c.C897G	D299E
c.898 C>T	c.C898T	L300F
c.899 T>C	c.T899C	L300P
c.901 C>G	c.C901G	R301G
c.902 G>C	c.G902C	R301P
c.902 G>A	c.G902A	R301Q
c.902 G>T	c.G902T	R301L
c.908 T>A	c.T908A	I303N
c.911 G>A	c.G911A	S304N
c.911 G>C	c.G911C	S304T
c.919 G>A	c.G919A	A307T
c.924 A>T	c.A924T	K308N
c.925 G>C	c.G925C	A309P
c.928 C>T	c.C928T	L310F
c.931 C>G	c.C931G	L311V
c.935 A>G	c.A935G	Q312R
c.936 G>T	c.G936T	Q312H
c.937 G>T	c.G937T	D313Y
c.938 A>G	c.A938G	D313G
c.946 G>A	c.G946A	V316I
c.947 T>G	c.T947G	V316G
c.950 T>C	c.T950C	I317T
c.955 A>T	c.A955T	I319F
c.956 T>C	c.T956C	I319T
c.959 A>T	c.A959T	N320I
c.962 A>G	c.A962G	Q321R
c.962 A>T	c.A962T	Q321L
c.963 G>C	c.G963C	Q321H
c.964 G>A	c.G964C	D322N
c.966 C>A	c.C966A	D322E

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.973 G>A	c.G973A	G325S
c.973 G>C	c.G973C	G325R
c.979 C>G	c.C979G	Q327E
c.983 G>C	c.G983C	G328A
c.1001 G>A	c.G1001A	G334E
c.1012 G>A	c.G1012A	E338K
c.1016 T>A	c.T1016A	V339E
c.1028 C>T	c.C1028T	P343L
c.1033 T>C	c.T1033C	S345P
c.1046 G>C	c.G1046C	W349S
c.1055 C>T	c.C1055T	A352V
c.1061 T>A	c.T1061A	I354K
c.1066 C>G	c.C1066G	R356G
c.1066 C>T	c.C1066T	R356W
c.1067G>A	c.G1067A	R356Q
c.1073 A>C	c.A1073C	E358A
c.1073 A>G	c.A1073G	E358G
c.1074 G>T	c.G1074T	E358D
c.1076 T>C	c.T1076C	I359T
c.1078 G>A	c.G1078A	G360S
c.1078 G>T	c.G1078T	G360C
c.1079 G>A	c.G1079A	G360D
c.1082 G>A	c.G1082A	G361E
c.1082 G>C	c.G1082C	G361A
c.1084 C>A	c.C1084A	P362T
c.1085 C>T	c.C1085T	P362L
c.1087 C>T	c.C1087T	R363C
c.1088 G>A	c.G1088A	R363H
c.1102 G>A	c.G1102A	A368T
c.1117 G>A	c.G1117A	G373S
c.1153 A>G	c.A1153G	T385A
c.1172 A>C	c.A1172C	K391T

Amenable *GLA* Mutations *(assumes 150 mg dose of migalastat HCl)*		
Nucleotide Change	**Nucleotide Change**	**Protein Sequence Change**
c.1184 G>A	c.G1184A	G395E
c.1184 G>C	c.G1184C	G395A
c.1192 G>A	c.G1192A	E398K
c.1202 Ins GACTTC	c.1202Ins GACTTC	p. T400_S401dup
c.1208 T>C	c.T1208C	L403S
c.1225 C>G	c.C1225G	P409A
c.1225 C>T	c.C1225T	P409S
c.1225 C>A	c.C1225A	P409T
c.1228 A>G	c.A1228G	T410A
c.1229 C>T	c.C1229T	T410I
c.1232 G>A	c.G1232A	G411D
c.1235 C>A	c.C1235A	T412N
c.1253 A>G	c.A1253G	E418G
c.1261 A>G	c.A1261G	M421V

The number of ‘GLA mutations that met the HEK-293 cell-based assay criteria’ is 268 of 841 in total.

Table 11SB:

The Pharmacogenetic Reference Table Based on the GLP HEK assay Results

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.1 A>C	*c.A1C*	*M1L*
c.1 A>G	*c.A1G*	*M1V*
c.2 T>G	*c.T2G*	*M1R*
c.2 T>C	*c.T2C*	*M1T*
c.2 T>A	*c.T2A*	*M1K*
c.3 G>A	*c.G3A*	*M1I*
c.19 G>T	*c.G19T*	*E7X#*
c.41 T>C	*c.T41C*	*L14P*
c.43 G>C	*c.G43C*	*A15P*
c.47 T>A	*c.T47A*	*L16H*
c.47 T>C	*c.T47C*	*L16P*
c.53 T>C	*c.T53C*	*F18S*
c.56 T>A	*c.T56A*	*L19Q*
c.56 T>C	*c.T56C*	*L19P*
c.59 C>T	*c.C59T*	*A20V*
c.61C>T	*c.C61T*	*L21F*
c.62 T>C	*c.T62C*	*L21P*
c.62 T>G	*c.T62G*	*L21R*
c.71 G>A	*c.G71A*	*W24X#*
c.92 C>T	*c.C92T*	*A31V*
c.118 C>G	*c.C118G*	*P40A*
c.118 C>T	*c.C118T*	*P40S*
c.119 C>A	*c.C119A*	*P40H*
c.119 C>G	*c.C119G*	*P40R*
c.119 C>T	*c.C119T*	*P40L*
c.127 G>C	*c.G127C*	*G43R*
c.127 G>A	*c.G127A*	*G43S*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.128 G>A	*c.G128A*	*G43D*
c.128 G>T	*c.G128T*	*G43V*
c.131 G>A	*c.G131A*	*W44X*[#]
c.132 G>T	*c.G132T*	*W44C*
c.134 T>C	*c.T134C*	*L45P*
c.134 T>G	*c.T134G*	*L45R*
c.134_138delTGCACinsGCTCG	c.134_138delTGCACinsGCTCG	*L45R/H46S*
c.136 C>T	*c.C136T*	*H46Y*
c.137 A>T	*c.A137T*	*H46L*
c.137 A>G	*c.A137G*	*H46R*
c.139 T>G	*c.T139G*	*W47G*
c.140 G>A or 141 G>A	*c.G140A or G141A*	*W47X*[#]
c.140 G>T	*c.G140T*	*W47L*
c.141G>C	*c.G141C*	*W47C*
c.139T>C	*c.T139C*	*W47R*
c.142 G>A	*c.G142A*	*E48K*
c.144 G>T	*c.G144T*	*E48D*
c.145 C>T	*c.C145T*	*R49C*
c.145 C>A	*c.C145A*	*R49S*
c.146 G>T	*c.G146T*	*R49G*
c.146 G>C	*c.G146C*	*R49P*
c.146 G>T	*c.G146T*	*R49L*
c.149 T>G	*c.T149G*	*F50C*
c.154 T>G	*c.T154G*	*C52G*
c.154 T>C	*c.T154C*	*C52R*
c.155 G>C	*c.G155C*	*C52S*
c.155 G>A	*c.G155A*	*C52Y*
c.156 C>A	*c.C156A*	*C52X*[#]
c.156 C>G	*c.C156G*	*C52W*
c.166 T>G	*c.T166G*	*C56G*
c.167 G>C	*c.G167C*	*C56S*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.168 C>A	*c.C168A*	*C56X#*
c.187 T>C	*c.T187C*	*C63R*
c.188 G>A	*c.G188A*	*C63Y*
c.188 G>C	*c.G188C*	*C63S*
c.194 G>C (putative splicing site)*	*c.G194C (putative splicing site*)*	*UNKNOWN (S65T*)#*
c.194 G>T (putative splicing site)*	*c.G194T (putative splicing site*)*	*UNKNOWN (S65I*)#*
c.196 G>C	*c.G196C*	*E66Q*
c.202 C>T	*c.C202T*	*L68F*
c.215 T>G	*c.T215G*	*M72R*
c.218 C>A	*c.C218A*	*A73E*
c.227 T>G	*c.T227G*	*M76R*
c.233 C>G	*c.C233G*	*S78X#*
c.235 G>T	*c.G235T*	*E79X#*
c.241 T>C	*c.T241C*	*W81R*
c.242 G>A	*c.G242A*	*W81X#*
c.242 G>C	*c.G242C*	*W81S*
c.243 G>T	*c.G243T*	*W81C*
c.244 A>T	*c.A244T*	*K82X#*
c.256 T>G	*c.T256G*	*Y86D*
c.256 T>C	*c.T256C*	*Y86H*
c.257 A>G	*c.A257G*	*Y86C*
c.258 T>G	*c.T258G*	*Y86X#*
c.262 T>G	*c.T262G*	*Y88D*
c.266 T>C	*c.T266C*	*L89P*
c.266 T>G	*c.T266G*	*L89R*
c.268 T>C	*c.T268C*	*C90R*
c.269 G>A	*c.G269A*	*C90Y*
c.270 C>A	*c.C270A*	*C90X#*
c.274 G>C	*c.G274C*	*D92H*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.274 G>A	*c.G274A*	*D92N*
c.274 G>T	*c.G274T*	*D92Y*
c.275 A>G	*c.A275G*	*D92G*
c.275 A>T	*c.A275T*	*D92V*
c.277 G>A	*c.G277A*	*D93N*
c.277 G>T	*c.G277T*	*D93Y*
c.278 A>G	*c.A278G*	*D93G*
c.278 A>T	*c.A278T*	*D93V*
c.279 C>G	*c.C279G*	*D93E*
c.281 G>C	*c.G281C*	*C94S*
c.281 G>A	*c.G281A*	*C94Y*
c.284 G>A	*c.G284A*	*W95X*[#]
c.284 G>T	*c.G284T*	*W95L*
c.284 G>C	*c.G284C*	*W95S*
c.295 C>T	*c.C295T*	*Q99X*[#]
c.299 G>A	*c.G299A*	*R100K*
c.299 G>C	*c.G299C*	*R100T*
c.305 C>G	*c.C305G*	*S102X*[#]
c.307 G>C	*c.G307C*	*E103Q*
c.307 G>T	*c.G307T*	*E103X*[#]
c.317 T>G	*c.T317G*	*L106R*
c.319 C>T	*c.C319T*	*Q107X*[#]
c.320 A>T	*c.A320T*	*Q107L*
c.334 C>T	*c.C334T*	*R112C*
c.334 C>A	*c.C334A*	*R112S*
c.338 T>C	*c.T338C*	*F113S*
c.350 T>G	*c.T350G*	*I117S*
c.355 C>T	*c.C355T*	*Q119X*[#]
c.358 C>G	*c.C358G*	*L120V*
c.[358 C>T; 359 T>C]	*c.C358T/T359C*	*L120S*
c.359 T>C	*c.T359C*	*L120P*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.361 G>C	*c.G361C*	*A121P*
c.371 T>A	*c.T371A*	*V124D*
c.374 A>C	*c.A374C*	*H125P*
c.379 A>T	*c.A379T*	*K127X*[#]
c.386 T>C	*c.T386C*	*L129P*
c.389 A>G	*c.A389G*	*K130R*
c.392 T>C	*c.T392C*	*L131P*
c.394 G>A	*c.G394A*	*G132R*
c.395 G>A	*c.G395A*	*G132E*
c.395 G>C	*c.G395C*	*G132A*
c.400 T>C	*c.T400C*	*Y134H*
c.400 T>G	*c.T400G*	*Y134D*
c.401 A>C	*c.A401C*	*Y134S*
c.402 T>G	*c.T402G*	*Y134X*[#]
c.406 G>C	*c.G406C*	*D136H*
c.406 G>T	*c.G406T*	*D136Y*
c.412 G>A	*c.G412A*	*G138R*
c.413 G>A	*c.G413A*	*G138E*
c.416 A>C	*c.A416C*	*N139T*
c.422 C>A	*c.C422A*	*T141N*
c.422 C>T	*c.C422T*	*T141I*
c.424 T>C	*c.T424C*	*C142R*
c.425 G>A	*c.G425A*	*C142Y*
c.426 C>A	*c.C426A*	*C142X*[#]
c.426 C>G	*c.C426G*	*C142W*
c.427 G>C	*c.G427C*	*A143P*
c.439 G>A	*c.G439A*	*G147R*
c.440 G>A	*c.G440A*	*G147E*
c.443 G>A	*c.G443A*	*S148N*
c.444 T>G	*c.T444G*	*S148R*
c.453 C>G	*c.C453G*	*Y151X*[#]

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.456 C>A	*c.C456A*	*Y152X#*
c.463 G>C	*c.G463C*	*D155H*
c.467 C>A	*c.C467A*	*A156D*
c.469 C>T	*c.C469T*	*Q157X#*
c.484 T>C	*c.T484C*	*W162R*
c.485 G>A	*c.G485A*	*W162X#*
c.485 G>T	*c.G485T*	*W162L*
c.486 G>C	*c.G486C*	*W162C*
c.488 G>T	*c.G488T*	*G163V*
c.491 T>G	*c.T491G*	*V164G*
c.493 G>T	*c.G493T*	*D165Y*
c.494 A>T	*c.A494T*	*D165V*
c.500 T>A	*c.T500A*	*L167Q*
c.500 T>C	*c.T500C*	*L167P*
c.503 A>G	*c.A503G*	*K168R*
c.504 A>C	*c.A504C*	*K168N*
c.508 G>A	*c.G508A*	*D170N*
c.508 G>C	*c.G508C*	*D170H*
c.509 A>G	*c.A509G*	*D170G*
c.509 A>T	*c.A509T*	*D170V*
c.511 G>C	*c.G511C*	*G171R*
c.511 G>T	*c.G511T*	*G171C*
c.512 G>A	*c.G512A*	*G171D*
c.514 T>G	*c.T514G*	*C172G*
c.514 T>C	*c.T514C*	*C172R*
c.515 G>C	*c.G515C*	*C172S*
c.515 G>T	*c.G515T*	*C172F*
c.515 G>A	*c.G515A*	*C172Y*
c.516 T>G	*c.T516G*	*C172W*
c.519 C>A	*c.C519A*	*Y173X#*
c.530 T>A	*c.T530A*	*L177X#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.547 G>A (putative splicing site)*	*c.G547A (putative splicing site*)*	*UNKNOWN (G183S*)*
c.548 G>T	*c.G548T*	*G183V*
c.557 A>C	*c.A557C*	*H186P*
c.560 T>G	*c.T560G*	*M187R*
c.572 T>C	*c.T572C*	*L191P*
c.605 G>A	*c.G605A*	*C202Y*
c.604 T>C	*c.T604C*	*C202R*
c.606 T>G	*c.T606G*	*C202W*
c.607 G>A	*c.G607A*	*E203K*
c.611 G>A or 612G>A	*c.G611A or G612A*	*W204X#*
c.612 G>T	*c.G612T*	*W204C*
c.614 C>G	*c.C614G*	*P205R*
c.617 T>C	*c.T617C*	*L206P*
c.620 A>G	*c.A620G*	*Y207C*
c.634 C>T	*c.C634T*	*Q212X#*
c.658 C>T	*c.C658T*	*R220X#*
c.661 C>T	*c.C661T*	*Q221X#*
c.666 C>A	*c.C666A*	*Y222X#*
c.667 T>G	*c.T667G*	*C223G*
c.667 T>C	*c.T667C*	*C223R*
c.668 G>A	*c.G668A*	*C223Y*
c.670 A>G	*c.A670G*	*N224D*
c.674 A>G	*c.A674G*	*H225R*
c.676 T>C	*c.T676C*	*W226R*
c.677 G>A	*c.G677A*	*W226X#*
c.678 G>T	*c.G678T*	*W226C*
c.679 C>T	*c.C679T*	*R227X#*
c.680 G>A	*c.G680A*	*R227Q*
c.680 G>C	*c.G680C*	*R227P*
c.688 G>A	*c.G688A*	*A230T*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.691 G>A	*c.G691A*	*D231N*
c.692 A>G	*c.A692G*	*D231G*
c.692 A>T	*c.A692T*	*D231V*
c.700 G>T	*c.G700T*	*D234Y*
c.702 T>G	*c.T702G*	*D234E*
c.704 C>A	*c.C704A*	*S235Y*
c.704 C>G	*c.C704G*	*S235C*
c.704 C>T	*c.C704T*	*S235F*
c.706 T>C	*c.T706C*	*W236R*
c.707 G>A	*c.G707A*	*W236X*[#]
c.707 G>T	*c.G707T*	*W236L*
c.708 G>C	*c.G708C*	*W236C*
c.712 A>C	*c.A712C*	*S238R*
c.718 A>T	*c.A718T*	*K240X*[#]
c.734 G>A or 735G>A	*c.G734A or G735A*	*W245X*[#]
c.739 T>C	*c.T739C*	*S247P*
c.748 C>T	*c.C748T*	*Q250X*[#]
c.751 G>T	*c.G751T*	*E251X*[#]
c.755 G>C	*c.G755C*	*R252T*
c.770 C>A	*c.C770A*	*A257D*
c.782 G>A	*c.G782A*	*G261D*
c.782 G>T	*c.G782T*	*G261V*
c.785 G>A	*c.G785A*	*W262X*[#]
c.785 G>T	*c.G785T*	*W262L*
c.786 G>C	*c.G786C*	*W262C*
c.791 A>C	*c.A791C*	*D264A*
c.791 A>T	*c.A791T*	*D264V*
c.793 C>T	*c.C793T*	*P265S*
c.794 C>G	*c.C794G*	*P265R*
c.796 G>C	*c.G796C*	*D266H*
c.796 G>T	*c.G796T*	*D266Y*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.796 G>A	*c.G796A*	*D266N*
c.797 A>C	*c.A797C*	*D266A*
c.797 A>T	*c.A797T*	*D266V*
c.798 T>A	*c.T798A*	*D266E*
c.800 T>G	*c.T800G*	*M267R*
c.801 G>A (putative splicing site)*	*c. G801A (putative splicing site*)*	*UNKNOWN (M267I*)*
c.803 T>C	*c.T803C*	*L268S*
c.806 T>A	*c.T806A*	*V269E*
c.811 G>T	*c.G811T*	*G271C*
c.812 G>T	*c.G812T*	*G271V*
c.815 A>G	*c.A815G*	*N272S*
c.816 C>A	*c.C816A*	*N272K*
c.819 T>G	*c.T819G*	*F273L*
c.820 G>A	*c.G820A*	*G274S*
c.821 G>T	*c.G821T*	*G274V*
c.823 C>T	*c.C823T*	*L275F*
c.826 A>G	*c.A826G*	*S276G*
c.830 G>A	*c.G830A*	*W277X*
c.835 C>A	*c.C835A*	*Q279K*
c.836 A>G	*c.A836G*	*Q279R*
c.837 G>C	*c.G837C*	*Q279H*
c.845 C>A	*c.C845A*	*T282N*
c.847 C>T	*c.C847T*	*Q283X#*
c.848 A>C	*c.A848C*	*Q283P*
c.848A>G	*c.A848G*	*Q283R*
c.853 G>C	*c.G853C*	*A285P*
c.854 C>A	*c.C854A*	*A285D*
c.859 T>G	*c.T859G*	*W287G*
c.860 G>A or 861G>A	*c.G860A or G861A*	*W287X#*
c.861 G>C	*c.G861C*	*W287C*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.863 C>A	*c.C863A*	*A288D*
c.865 A>T	*c.A865T*	*I289F*
c.874 G>A	*c.G874A*	*A292T*
c.874 G>C	*c.G874C*	*A292P*
c.875 C>T	*c.C875T*	*A292V*
c.877 C>G	*c.C877G*	*P293A*
c.877 C>T	*c.C877T*	*P293S*
c.878 C>A	*c. C878A*	*P293H*
c.878 C>T	*c. C878T*	*P293L*
c.881 T>G	*c.T881G*	*L294X#*
c.890 C>G	*c. C890G*	*S297C*
c.890 C>T	*c.C890T*	*S297F*
c.892 A>C	*c.A892C*	*N298H*
c.894 T>G	*c.T894G*	*N298K*
c.896 A>G	*c.A896G*	*D299G*
c.899 T>A	*c.T899A*	*L300H*
c.901 C>T	*c.C901T*	*R301X#*
c.916 C>T	*c.C916T*	*Q306X#*
c.929 T>G	*c.T929G*	*L310R*
c.931 C>T	*c.C931T*	*L311F*
c.932 T>C	*c.T932C*	*L311P*
c.932 T>G	*c.T932G*	*L311R*
c.947 T>A	*c.T947A*	*V316E*
c.950 T>A	*c.T950A*	*I317N*
c.950 T>G	*c.T950G*	*I317S*
c.958 A>T	*c.A958T*	*N320Y*
c.960 T>G	*c.T960G*	*N320K*
c.961 C>G	*c.C961G*	*Q321E*
c.961 C>T	*c.C961T*	*Q321X#*
c.974 G>A	*c.G974A*	*G325D*
c.979 C>A	*c.C979A*	*Q327K*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.982 G>A	*c.G982A*	*G328R*
c.982 G>T	*c.G982T*	*G328W*
c.983 G>A	*c.G983A*	*G328E*
c.983 G>T	*c.G983T*	*G328V*
c.988 C>T	*c.C988T*	*Q330X*[#]
c.997 C>T	*c.C997T*	*Q333X*[#]
c.998 A>G	*c.A998G*	*Q333R*
c.1012 G>T	*c.G1012T*	*E338X*[#]
c.1016 T>G	*c.T1016G*	*V339G*
c.1018 T>C	*c.T1018C*	*W340R*
c.1020 G>A	*c.G1020A*	*W340X*[#]
c.1021 G>A	*c.G1021A*	*E341K*
c.1023 A >C	*c.A1023C*	*E341D*
c.1024 C>T	*c.C1024T*	*R342X*[#]
c.1025 G>A	*c.G1025A*	*R342Q*
c.1025 G>C	*c.G1025C*	*R342P*
c.1025 G>T	*c.G1025T*	*R342L*
c.1031 T>C	*c.T1031C*	*L344P*
c.1034 C>G	*c.C1034G*	*S345X*[#]
c.1042 G>C	*c.G1042C*	*A348P*
c.1045 T>C	*c.T1045C*	*W349R*
c.1046 G>A	*c.G1046A*	*W349X*[#]
c.1048 G>C	*c.G1048C*	*A350P*
c.1054 G>C	*c.G1054C*	*A352P*
c.1055 C>A	*c.C1055A*	*A352D*
c.1065 C>A	*c.C1065A*	*N355K*
c.1069 C>T	*c.C1069T*	*Q357X*
c.1072 G>A	*c.G1072A*	*E358K*
c.1081 G>A	*c.G1081A*	*G361R*
c.1088 G>C	*c.G1088C*	*R363P*
c.1095 T>A	*c.T1095A*	*Y365X*[#]

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.1115 T>A	*c.T1115A*	*L372Q*
c.1115 T>C	*c.T1115C*	*L372P*
c.1115 T>G	*c.T1115G*	*L372R*
c.1117 G>C	*c.G1117C*	*G373R*
c.1118 G>A	*c.G1118A*	*G373D*
c.1124_1129del	*c.1124_1129del*	*G375_V376del*
c.1129_1140dup	*c.1129_1140dup*	*A377_P380dup*
c.1130 C>A	*c.C1130A*	*A377D*
c.1132 T>C	*c.T1132C*	*C378R*
c.1133 G>A	*c.G1133A*	*C378Y*
c.1145 G>A	*c.G1145A*	*C382Y*
c.1146 C>G	*c.C1146G*	*C382W*
c.1151 T>A	*c.T1151A*	*I384N*
c.1153 A>C	*c.A1153C*	*T385P*
c.1156 C>T	*c.C1156T*	*Q386X*[#]
c.1157 A>C	*c.A1157C*	*Q386P*
c.1165 C>G	*c.C1165G*	*P389A*
c.1166 C>G	*c.C1166G*	*P389R*
c.1166 C>T	*c.C1166T*	*P389L*
c.1181_1183dup	*c.1181_1183dup*	*L394_G395InsV*
c.1187 T>A	*c.T1187A*	*F396Y*
c.1192 G>T	*c.G1192T*	*E398X*[#]
c.1196 G>A or1197 G>A	*c.G1196A or G1197A*	*W399X*
c.1202 C>G	*c.C1202G*	*S401X*[#]
c.1215 T>A	*c.T1215A*	*S405R*
c.1217 A>G	*c.A1217G*	*H406R*
c.1219 A>G	*c.A1219G*	*I407V*
c.1220 T>A	*c.T1220A*	*I407K*
c.1220 T>G	*c.T1220G*	*I407R*
c.1228 A>C	*c.A1228C*	*T410P*
c.1229 C>A	*c.C1229A*	*T410K*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.1241 T>C	*c.T1241C*	*L414S*
c.1243 C>T	*c.C1243T*	*L415F*
c.1244 T>C	*c.T1244C*	*L415P*
c.1246 C>T	*c.C1246T*	*Q416X*
c.1250 T>G	*c.T1250G*	*L417R*
g.941_5845del	*c.1-179_369+577del*	*p.?(Exon1_2del)#*
g.?_?del	*c.?_?*	*UNKNOWN (del Exon1_2?)#*
c.18delA	*c.18delA*	*p.P6fs*114#*
c.26delA	*c.26delA*	*p.H9Lfs*111#*
c.32delG	*c.32delG*	*p.G11Afs*109#*
c.33delC	*c.33delC*	*p.G11fs*109#*
c.34_42del	*c.34_42del*	*p.C12_L14del*
c.34_57del	*c.34_57del*	*p.C12_L19del*
c.35_47del	*c.35_47del*	*p.C12Ffs*104#*
c.147_148 Ins CCC	*c.147_148 Ins CCC*	*p.49Ins P*
c.58_83del	*c.58_83del*	*p.A20_G28delfs*2#*
c.58_72del	*c.58_72del*	*p.A20_W24del*
c.85dupG	*c.85dupG*	*p.A29Gfs*1#*
c.123delC	*c.123delC*	*p.T41fs*79#*
c.123_126dupCATG	*c.123_126dupCATG*	*p.G43Hfs*13#*
c.124_125del	*c.124_125del*	*p.M42Gfs*12#*
c.125_137del	*c.125_137del*	*p.M42Tfs*74#*
c.154delT	*c.154delT*	*p.C52Afs*68#*
c.162delT	*c.162delT*	*p.L54fs*66#*
c.181_182dupA	*c.181_182dupA*	*p.D61Efs*5#*
c.184delT	*c.184delT*	*p.S62Pfs*58#*
g.2594_10904dup	*c.195-2500_999+197dup*	*UNKNOWN#*
g.3422_6041delinsCG	*c.194+2049_369+773del2620ins CG*	*UNKNOWN#*
g.?_?del	*c.195-?_547+?del*	*UNKNOWN (del Exon2_3?)#*
g.?_?dup	*c.?_?dup*	*UNKNOWN (Exon2_4dup?)#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
g.2934_6378del	*c.194+1561_370-891del*	*UNKNOWN (E66_Y123del; del Exon2?)#*
g.3396_6012del	*c.194+2023_370-1257del*	*UNKNOWN (E66_Y123del; del Exon2?)#*
g.3260_6410del	*c.194+1887_370-859del*	*UNKNOWN (E66_Y123del; del Exon2?)#*
g.2979_6442del	*c.194+1606_369+1174del*	*UNKNOWN (E66_Y123del; del Exon2)#*
c.256delT	*c.256delT*	*p.Y88Mfs*42#*
g.5106_5919delins231	*c.207_369+651del814ins231*	*UNKNOWN (del Exon2?)#*
c.259_276Del	*c.259_276 Del*	*p.87_92del*
c.267_268dupCT	*c.267_268dupCT*	*p.C90Sfs*31#*
c.270delC	*c.270delC*	*p.C90X#*
c.281_286delinsT	*c.281_286delinsT*	*p.C94Ffs*26#*
c.297_298del	*c.297_298del*	*p.Q99fs*22#*
c.305delC	*c.305delC*	*p.S102X#*
c.317_327del	*c.317_327del*	*p.S102fs*16#*
c.323_324insCAGA	*c.323_324insCAGA*	*p.D109Rfs*14#*
c.336 Del18	*c.336 Del18*	*p.113del6aa*
c.358 Del6	*c.358 Del6*	*p.120del2aa/L120H*
c.363delT	*c.363delT*	*p.A121fs*8#*
g.5271_9366del4096insT	*c.369+3_639+954del3129insT*	*UNKNOWN (del Exon3 and 4?)#*
g.7086_7487del	*c.370-183_547+41del*	*UNKNOWN (del Exon3?)#*
g.6736_11545del	*c.370-533_c.1290+277del*	*UNKNOWN (del Exon3_7?)#*
g.6009_9741del	*c.369+741_640-390del*	*UNKNOWN (del Exon3 and 4?)#*
g.6547_9783del	*c.369+1279_640-348del*	*UNKNOWN (del Exon3 and 4?)#*
g.>5.5 kb del to 3UTR	*c.?_?del*	*UNKNOWN (del Exon3_3'UTR?)#*
c.[374 A>T;383 G>A]	*c.A374T/G383A*	*H125L/G128E*
c.402delT	*c.402delT*	*p.Y134X#*
c.409delG	*c.409delG*	*p.V137Lfs*27#*
c.413dupG	*c.413dupG*	*p.G138fs*2#*
c.421delA	*c.421delA*	*p.T141Pfs*23#*
c.426dupC	*c.426dupC*	*p.A143Rfs*13#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.452delA	*c.452delA*	*p.Y151Sfs*13#*
c.457_459del	*c.457_459del*	*p.153delD*
c.477delT	*c.477delT*	*p.F159Lfs*5#*
c.486_498del	*c.486_498del*	*p.W162Cfs*1#*
c.516 InsGAC	*c.516 InsGAC*	*p. 152 Ins D*
c.520delT	*c.520delT*	*p.C174Vfs*17#*
c.[604 T>C;644 A>G]	*c.T604C/A644G*	*p. C202R/N215S*
c.568delG	*c.568delG*	*p.A190Pfs*1#*
c.590delG	*c.590delG*	*p.S197Tfs*42#*
c.606delT	*c.606delT*	*p.C202Wfs*37#*
c.613_621del	*c.613_621del*	*p.205_207del*
c.614delC	*c.614delC*	*p.P205Lfs*34#*
c.618_619del	*c.618_619del*	*p.L206fs*24#*
c.621dupT	*c.621dupT*	*p.M208Yfs*24#*
g.?_?del	*c.?_?del*	*UNKNOWN (del Exon5_7?)#*
g.[10237_11932del; 11933_12083inv; 12084_12097del]	*g.[10237_11932del; 11933_12083inv; 12084_12097del]*	*UNKNOWN#*
c.646dupT	*c.646dupT*	*p.Y216Lfs*15#*
c.646delT	*c.646delT*	*p.Y216Ifs*23#*
c.650_663dup14	*c.650_663dup14*	*p.Q221fs*23#*
c.672_673ins37	*c.672_673ins37*	*p.H225Tfs*18#*
c.674_732del	*c.674_732del*	*p.H225Lfs*5#*
c.678delG	*c.678delG*	*p.A230Lfs*9#*
c.715_717 del	*c.715_717 del*	*p.del I239*
c.716dupT	*c.716dupT*	*p.I239fs*10#*
c.718_719del	*c.718_719del*	*p.K240Efs*8#*
c.719dupA	*c.719dupA*	*p.K240fs*9#*
c.722delG	*c.722delG*	*p.S241Ifs*27#*
c.723dupT	*c.723dupT*	*p.S238fs*8#*
c.732delC	*c.732delC*	*p.D244fs*24#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.741ins9	*c.741ins9*	*p.247ins3*
c.744delT	*c.744delT*	*p.F248Lfs*20#*
c.744_745del	*c.744_745del*	*p.F248Lfs*6#*
c.746_747del	*c.746_747del*	*p.N249Tfs*5#*
c.759delT	*c.759delT*	*p.I253Mfs*15#*
c.760dupG	*c.760dupG*	*p.V254Gfs*1#*
c.761_762del	*c.761_762del*	*p.V254Gfs*9#*
c.774_775del	*c.774_775del*	*p.G258fx*5#*
c.777delA	*c.777delA*	*p.P259fs*9#*
c.782dupG	*c.782dupG*	*p.G261fs*3#*
c.807delG	*c.807delG*	*p.V269fs*12#*
c.833dupA	*c.833dupA*	*p.N278Kfs*20#*
c.833delA	*c.833delA*	*p.N278Ifs*3#*
c.842_844del	*c.842_844del*	*p.V281AdelT282*
c.881delT	*c.881delT*	*p.L294Yfs*22#*
c.892_893insT	*c.892_893insT*	*p.N298I*1#*
c.893_894insG	*c.893_894insG*	*p.N298Kfs*1#*
c.902dupG	*c.902dupG*	*p.R301fs*13#*
c.909_918del	*c.909_918del*	*p.I303Mfx*10#*
c.914delC	*c.914delC*	*p.P305Lfs*11#*
c.931delC	*c.931delC*	*p.L311Ffs*5#*
c.941_961del	*c.941_961del*	*p.D315_Q321del*
c.946delG	*c.946delG*	*p.V316X#*
c.950_954dupTTGCC	*c.950_954dupTTGCC*	*p.A318fs*31#*
c.974dupG	*c.974dupG*	*p.G325fs*7#*
c.986delA	*c.986delA*	*p.Y329Sfs*18#*
c.988delC	*c.988delC*	*p.Q330Sfs*17#*
c.946_966del	*c.946_966del*	*p.V316_D322del*
c.994delA	*c.994delA*	*p.R332Dfs*15#*
c.996_999del	*c.996_999del*	*p.R332fs*14#*
c.997dupC	*c.997dupC*	*p.Q333Pfs*5#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.1011_1029del	*c.1011_1029del*	*p.F337fs*4#*
c.1017_1020delins24	*c.1017_1020delins24*	*p.V339fs*7#*
c.1017_1027del	*c.1017_1027del*	*p.V339fs*5#*
c.1021delG	*c.1021delG*	*p.E341Nfs*6#*
c.1025delG	*c.1025delG*	*p.R342Hfs*5#*
c.1030_1031insT	*c.1030_1031insT*	*p.L344fs*30#*
c.1033_1034del	*c.1033_1034del*	*p.S345Rfs*28#*
c.1037delG	*c.1037delG*	*p.G346Afs*1#*
c.1040dupT	*c.1040dupT*	*p.L347Ffs*27#*
c.1041dupA	*c.1041dupA*	*p.L347fs*27#*
c.1042dupG	*c.1042dupG*	*p.A348Gfs*26#*
c.1043_1044insG	*c.1043_1044insG*	*p.A348fs*26#*
c.1049delC	*c.1049delC*	*p.A350Vfs*1#*
c.1151_1152delinsAT	*c.1151_1152delinsAT*	*p.I384N*
c.1055_1057dup	*c.1055_1057dup*	*p.353InsT*
c.1057_1058del	*c.1057_1058del*	*p.M353Dfs*20#*
c.1072_1074del	*c.1072_1074del*	*p.358delE*
c.1074_1075del	*c.1074_1075del*	*p.E358Dfs*15#*
c.1077delT	*c.1077delT*	*p.I359Mfs*31#*
c.1081_1100del	*c.1081_1100del*	*p.G360fs*7#*
c.1086_1098del	*c.1086_1098del*	*p.P362fs*24#*
c.1088delG	*c.1088delG*	*p.R363Pfs*27#*
c.1091_1092del	*c.1091_1092del*	*p.S364Lfs*9#*
c.1093dupT	*c.1093dupT*	*p.Y365Lfs*9#*
c.1095delT	*c.1095delT*	*p.Y365X#*
c.1096_1100del	*c.1096_1100del*	*p.Y365fs*7#*
c.1102delGinsTTATAC	*c.1102delGinsTTATAC*	*p.A368delinsFYfs*23#*
c.1122_1125del	*c.1122_1125del*	*p.K374fs*15#*
c.1123_1175del	*c.1123_1175del*	*p.G375_R392del*
c.1139delC	*c.1139delC*	*p.380Lfs*10#*
c.1145_1149del	*c.1145_1149del*	*p.C382Yfs*14#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
c.1146_1148del	*c.1146_1148del*	*p.383delF*
c.1156_1157del	*c.1156_1157del*	*p.Q386Afs*10#*
c.1167dupT	*c.1167dupT*	*p.P389fs*9#*
c.1168 Ins T	*c.1168 Ins T*	*p. V390fs*9*
c.1176_1179del	*c.1176_1179del*	*p.R392Sfs*1#*
c.1177_1178del	*c.1177_1178del*	*p.K393Afs*4#*
c.1187dupT	*c.1187dupT*	*p.F396fs*2#*
c.1187delT	*c.1187delT*	*p.F396Sfs*7#*
c.1188delC	*c.1188delC*	*p.F396fs*7#*
c.1201dupT	*c.1201dupT*	*p.S401Ffs*49#*
c.1208delT	*c.1208delT*	*p.L403X#*
c.1208ins21	*c.1208ins21*	*UNKNOWN#*
c.1209_1211del	*c.1209_1211del*	*p.404delR*
c.1223delA	*c.1223delA*	*p.N408Ifs*9*
c.1235_1236del	*c.1235_1236del*	*p.T412Sfs*37*
c.1277_1278del	*c.1277_1278del*	*p.K426Rfs*23*
c.1284_1287del	*c.1284_1287del*	*p.L428Ffs*23*
c.359 T>C; c.361 G>A	*c.T359C/G361A*	*L120P/A121T*
c.644 A>G; c.811 G>A	*c.A644G; c.G811A*	*N215S/G271S*
c.[644 A>G; 811 G>A; 937 G>T]	*c.A644G/G811A/G937T*	*N215S/G271S/D313Y*
c.790 G>T; c.805 G>A	*c.G790T/G805A*	*D264Y/V269M*
c.963_964 GG>CA	*c.G963C/G964C*	*Q321H/D322N*
c.1288 T>C	*c. T1288C*	*X430Q*
IVS1+2 T>C	*c.194+2 T>C*	*UNKNOWN#*
IVS1-1 G>A	*c.195-1 G>A*	*UNKNOWN#*
IVS1-1 G>T	*c.195-1 G>T*	*UNKNOWN#*
IVS1-2 A>G	*c.195-2 A>G*	*UNKNOWN#*
IVS1-2 A>G;IVS1-49 T>C	*c.[195-2 A>G;195-49 T>C]*	*UNKNOWN#*
IVS2+1 G>A	*c.369+1 G>A*	*UNKNOWN#*
IVS2+2 T>G	*c.369+2 T>G*	*UNKNOWN#*

Non-amenable GLA Mutations (assume 150 mg dose of migalastat HCl)		
Nucleotide Change		***Protein Sequence Change***
IVS2-2 A>G	*c.370-2A>G*	*UNKNOWN*[#]
IVS3+1 G>A	*c.547+1 G>A*	*UNKNOWN*[#]
IVS3+1 G>C	*c.547+1 G>C*	*UNKNOWN*[#]
IVS3-2 A>G	*c.548-2 A>G*	*UNKNOWN*[#]
IVS3-1 G>A	*c.548-1 G>A*	*UNKNOWN*[#]
IVS3-1 G>C	*c.548-1 G>C*	*UNKNOWN*[#]
IVS3-1 G>T	*c.548-1 G>T*	*UNKNOWN*[#]
IVS4-1 G>T	*c.639-1 G>T*	*UNKNOWN*[#]
IVS4+1 G>A	*c.639+1 G>A*	*UNKNOWN*[#]
IVS4+1 G>C	*c.639+1 G>C*	*UNKNOWN*[#]
IVS4+4 A>T	*c.639+4 A>T*	*UNKNOWN*[#]
IVS4+861 C>T	*c.639+861 C>T*	*UNKNOWN*[#]
IVS4+919 G>A	*c.639+919G>A*	*UNKNOWN*[#]
IVS4-11 T>A	*c.640-11 T>A*	*UNKNOWN*[#]
IVS4-3 C>G	*c.640-3 C>G*	*UNKNOWN*[#]
IVS4-2 A>T	*c.640-2 A>T*	*UNKNOWN*[#]
IVS4-1 G>A	*c.640-1 G>A*	*UNKNOWN*[#]
IVS5+2 T>C	*c.801+2 T>C*	*UNKNOWN*[#]
IVS5+3 A>G	*c.801+3 A>G*	*UNKNOWN*[#]
IVS5+4 A>G	*c.801+4 A>G*	*UNKNOWN*[#]
IVS5-2 A>G	*c.802-2 A>G*	*UNKNOWN*[#]
IVS6+1 G>T	*c.999+1 G>T*	*UNKNOWN*[#]
IVS6+2 T>C	*c.999+2 T>C*	*UNKNOWN*[#]
IVS6-2 A>G	*c.1000-2 A>G*	*UNKNOWN*[#]
IVS6-2 A>T	*c.1000-2 A>T*	*UNKNOWN*[#]
IVS6-1 G>A	*c.1000-1 G>A*	*UNKNOWN*[#]
IVS6-1 G>C	*c.1000-1 G>C*	*UNKNOWN*[#]

[#]Mutation did not qualify for testing in the GLP HEK assay. Mutations that generally do not qualify for testing include large deletions, insertions, truncations, frameshift mutations, and splice site mutations. These types of mutations often lead to the loss of entire protein domains that grossly alter the structure and function of the enzyme, and may even result in the complete loss of expression. Splice site mutations, in particular, can lead to incorrect processing of mRNA precursors, including exon skipping or splicing at cryptic splice points, resulting in gross

structural and functional alterations. Furthermore, splice site mutations are not testable in the GLP HEK assay because this assay uses recombinant *GLA* cDNA; thus, the mutant α-Gal A is expressed independent of pre-mRNA splicing. Mutations that do not qualify for testing in the GLP HEK assay are categorized as non-amenable without testing.

*While these nucleotide changes cause apparent single amino acid residue substitutions (as indicated in the parenthesis in the column of 'protein sequence change'), scientific evidence [3] indicate that these are putative splicing mutations that cause gross changes to α-Gal A protein sequences.

Question marks (?) in the columns of 'Nucleotide Change' indicate that the underlying mutations were not reported in the literature and therefore are not available.
UNKNOWN in the column of 'protein sequence change' indicate that the changes to the protein sequence caused by the mutations cannot be readily deduced from the nucleotide changes and need to be experimentally determined. In these cases, the question marks in the accompanying parentheses indicate that the changes provided therein have not been experimentally confirmed and may not be correct.

Two or more nucleotide changes that lead to the same stop codon indicate that more than one patient each with a different *GLA* mutation leading to the same nonsense mutant form of α-Gal A has been reported.
Notes to the pharmacogenetic reference table:

- Amenable mutations are defined as those in *GLA* that translate to mutant forms of the enzyme with α Gal A activity in the presence of 10 μM migalastat that is ≥1.20-fold over baseline and an absolute increase at 10 μM migalastat of ≥3.0% of wild-type α Gal A activity.
- The results listed in this table are based on GLP HEK-293 cell-based assay. Mutations may change in category if scientific evidence suggests that the mutations may lead to forms of the α-Gal A protein *in vivo* that are different from those expected based solely on the cDNA sequence.

References

1. Wu X, Katz E, Valle CD, et al. A pharmacogenetic approach to identify mutant forms of α-galactosidase A that respond to a pharmacological chaperone for Fabry disease. *Hum. Mutat.* 2011;32(8):965-977.
2. Johnson FK, Mudd PN, Bragat A, Adera M, Boudes P. Pharmacokinetics and Safety of Migalastat HCl and Effects on Agalsidase Activity in Healthy Volunteers. *Clin Pharmacol Drug Dev.* 2013;2(2):120-132.
3. Lai LW, Whitehair O, Wu MJ, O'Meara M, Lien YH. Analysis of splice-site mutations of the α-galactosidase A gene in Fabry disease. *Clin. Genet.* 2003;63(6):476-482.