2 SYNOPSIS

<table>
<tr><td>NAME OF COMPANY:
Amicus Therapeutics, Inc.</td><td colspan="2">INDIVIDUAL STUDY SYNOPSIS</td></tr>
<tr><td>NAME OF FINISHED PRODUCT:
Not Applicable

NAME OF ACTIVE INGREDIENT:
AT1001 (migalastat hydrochloride)</td><td>INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER
Volume:

Page:</td><td>(FOR NATIONAL AUTHORITY USE ONLY)</td></tr>
<tr><td colspan="3">Title of Study: An open-label Phase 2a study to investigate drug-drug interactions between AT1001 (migalastat hydrochloride) and agalsidase in subjects with Fabry disease</td></tr>
<tr><td colspan="3">Protocol Number: AT1001-013</td></tr>
<tr><td colspan="3">Investigators:
Gabor E. Linthorst, MD, PhD; Suma Shankar, MD; Majed Dasouki, MD; Ozlem Goker-Alpan, MD; David G. Warnock, MD; Myrl Holida, PA-C; Francois Eyskens, MD; Kathleen Nicholls, MD; Mark Thomas, MD; and Daniel Bichet, MD</td></tr>
<tr><td colspan="3">Study Sites: The following 10 sites enrolled subjects:
• Site 1802, G. Linthorst, Amsterdam, The Netherlands
• Site 2001, S. Shankar, Decatur, GA, USA
• Site 2008, M. Dasouki, Kansas City, KS, USA
• Site 2017, O. Goker-Alpan, Fairfax, VA, USA
• Site 2018, D. Warnock, Birmingham, AL, USA
• Site 2019, M. Holida, Iowa City, IA, USA
• Site 2601, F. Eyskens, Edegem, Belgium
• Site 4001, K. Nicholls, Parkville, VIC, Australia
• Site 4003, M. Thomas, Perth, WA, Australia
• Site 6001, D. Bichet, Montreal, QC, Canada</td></tr>
<tr><td colspan="3">Publication (Reference): None</td></tr>
<tr><td colspan="2">Studied Period:
Date of first observation: 02 February 2011
Date of last observation: 09 October 2012</td><td>Phase of Development: 2a</td></tr>
<tr><td colspan="3">Objectives:
Primary Objectives:
• To characterize the effects of 150 mg and 450 mg of AT1001 (hereafter referred to as migalastat hydrochloride [HCl]) administered 2 hours before administration of agalsidase on the safety and plasma pharmacokinetics of agalsidase in subjects with Fabry disease
• To characterize the effect of agalsidase on the safety and plasma pharmacokinetics of 150 mg of migalastat HCl administered 2 hours before administration of agalsidase in subjects with Fabry disease</td></tr>
</table>

NAME OF COMPANY: Amicus Therapeutics, Inc.	**INDIVIDUAL STUDY SYNOPSIS**	
NAME OF FINISHED PRODUCT: Not Applicable **NAME OF ACTIVE INGREDIENT:** AT1001 (migalastat hydrochloride)	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(FOR NATIONAL AUTHORITY USE ONLY)

Secondary Objective:

- To characterize the effect of 150 mg and 450 mg migalastat HCl on the distribution of α-galactosidase A (α-Gal A) to skin after administration of agalsidase

Methodology: This open-label, non-randomized study consisted of 2 stages. Two dose levels of migalastat HCl (150 mg and 450 mg) were selected to evaluate interaction with each of the following doses of recombinant agalsidase: 0.2 mg/kg agalsidase alfa (Replagal®, Shire Human Genetic Therapies), 0.5 mg/kg agalsidase beta (Fabrazyme®, Genzyme Corporation), or 1.0 mg/kg agalsidase beta (Fabrazyme).

- Stage 1 of the study consisted of a screening visit and 3 treatment periods to evaluate the effect of 150 mg migalastat HCl on the pharmacokinetics and safety of agalsidase (0.2 mg/kg agalsidase alfa, 0.5 mg/kg agalsidase beta, or 1.0 mg/kg agalsidase beta), and the effect of agalsidase on the pharmacokinetics and safety of 150 mg migalastat
- Stage 2 consisted of a screening visit and 2 treatment periods to evaluate the effect of 450 mg migalastat HCl on the pharmacokinetics and safety of agalsidase (0.2 mg/kg agalsidase alfa, 0.5 mg/kg agalsidase beta, or 1.0 mg/kg agalsidase beta)

Subjects in each stage received each of the following treatments in the order described in the following table:

	Stage 1	**Stage 2**
Period 1	Intravenous infusion of 0.2 mg/kg agalsidase alfa, or 0.5 mg/kg or 1.0 mg/kg agalsidase beta	Intravenous infusion of 0.2 mg/kg agalsidase alfa, or 0.5 mg/kg or 1.0 mg/kg agalsidase beta
Period 2	A single 150 mg oral dose (1 capsule) of migalastat HCl 2 hours before initiation of an intravenous (IV) infusion of 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta	A single 450 mg oral dose (3 × 150-mg capsules) of migalastat HCl 2 hours before initiation of an IV infusion of 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta
Period 3	A single 150 mg oral dose (1 capsule) of migalastat HCl	---

The first 10 to 12 subjects (a minimum of 4 subjects receiving agalsidase alfa, and the remaining subjects receiving agalsidase beta) who met all eligibility criteria were to be enrolled into Stage 1. The decision to initiate dosing in Stage 2 was made by the Amicus medical monitor and investigators after consideration of safety and tolerability information from at least the first 4 subjects who had completed Stage 1. Subjects receiving agalsidase beta were assigned to Stage 2 after a minimum of 6 subjects had completed Stage 1. Subjects receiving agalsidase alfa were assigned to Stage 2 after a minimum of 4 subjects had completed Stage 1. In Stage 2, at least 4 subjects were to be treated with 450 mg migalastat HCl co-administered with each form of

NAME OF COMPANY: Amicus Therapeutics, Inc.	**INDIVIDUAL STUDY SYNOPSIS**	
NAME OF FINISHED PRODUCT: Not Applicable **NAME OF ACTIVE INGREDIENT:** AT1001 (migalastat hydrochloride)	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(FOR NATIONAL AUTHORITY USE ONLY)

enzyme replacement therapy (ERT): agalsidase alfa or beta.

Agalsidase alfa was administered as a 40-minute infusion, and agalsidase beta was administered as a 2-hour infusion. Every effort was made to ensure that the durations of the infusions during Periods 1 and 2 were the same. The following procedures/assessments took place at the time points specified in the Schedule of Assessments table: informed consent, medical history and demographic data, estimated glomerular filtration rate (eGFR), physical examination, 12-lead electrocardiogram (ECG), vital signs, concomitant medications, laboratory assessments (hematology, serum chemistry, coagulation profile, and urinalysis), urine globotriaosylceramide (GL-3)/ urine globotriaosylsphingosine (lyso-Gb_3), plasma lyso-Gb_3, pharmacokinetic (PK) blood sampling, skin biopsy, blood sampling for white blood cell (WBC) and plasma α–Gal A levels, antibody titer, and adverse events (AEs).

Number of Subjects:

Approximately 4 to 6 subjects using each form of agalsidase at each dose level were planned (ie, agalsidase beta + migalastat HCl 150 mg; agalsidase beta + migalastat HCl 450 mg; agalsidase alfa + migalastat HCl 150 mg; and agalsidase alfa + migalastat HCl 450 mg) for a possible total of 18 to 24 evaluable subjects.

Diagnosis and Main Criteria for Inclusion: Male subjects with Fabry disease between 18 and 65 years of age who had been receiving a stable dose (0.3-1.0 mg/kg) of agalsidase beta or (≥ 0.2 mg/kg) of agalsidase alfa for at least 1 month before study entry, who had received at least 2 infusions before the screening visit, and who had an estimated creatinine clearance ≥ 50 mL/min at screening, were enrolled into the study. A stable dose of enzyme was defined as a dose not varying by more than ± 20%.

Test Product, Dose, Mode of Administration, and Batch Number(s):

Migalastat HCl was administered as an oral dose of 150 mg during Stage 1 and as an oral dose of 450 mg during Stage 2.

Batch Numbers: E07889-001L01, E07889-002L01, E07889-003L01, E07889-005L1, and E07889-006L

Duration of Treatment: Up to 4.5 months

Reference Therapy, Dose, Mode of Administration, and Batch Number(s):

Agalsidase alfa was administered at a dose of 0.2 mg/kg, and agalsidase beta was administered at a dose of 0.5 mg/kg or 1.0 mg/kg; each was administered as an IV infusion using a calibrated infusion pump.

Commercially available agalsidase alfa (Replagal) and agalsidase beta (Fabrazyme) were used. As subjects were already on these drugs at study entry, the batch numbers were not collected.

NAME OF COMPANY: Amicus Therapeutics, Inc.	**INDIVIDUAL STUDY SYNOPSIS**	
NAME OF FINISHED PRODUCT: Not Applicable **NAME OF ACTIVE INGREDIENT:** AT1001 (migalastat hydrochloride)	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(FOR NATIONAL AUTHORITY USE ONLY)

Criteria for Evaluation:

Primary Endpoints:

- Agalsidase plasma PK parameter values by measurement of active α–Gal A levels (α–Gal A enzyme activity) and total α–Gal A protein levels after agalsidase infusion alone and in combination with oral migalastat HCl: area under the plasma concentration versus time curve (AUC) from time 0 to t_{last} (last time point at which concentration is quantified) (AUC_{0-t}), AUC extrapolated from time 0 to infinity ($AUC_{infinity}$), maximum observed plasma concentration (C_{max}), time to maximum observed plasma concentration (t_{max}), and terminal elimination half-life ($t_{½}$)
- Migalastat plasma PK parameter values after administration of a single oral dose of migalastat HCl alone and in combination with agalsidase: $AUC_{0–t}$, $AUC_{infinity}$, C_{max}, t_{max}, $t_{½}$
- Safety variables: AEs (including infusion site reactions), clinical laboratory assessments, 12-lead ECGs, physical examinations, and vital signs

Secondary Endpoint:

- Uptake of α-Gal A to skin after agalsidase alone and in combination with migalastat HCl at 24 hours and 7 days after dosing by measuring α–Gal A activity and total α–Gal A protein levels

Exploratory Endpoints:

- Urinary GL-3 excretion before and 14 days after each agalsidase dose
- The α–Gal A enzyme activity in WBCs, determined before initiation of the agalsidase infusion and at 2, 4, and 24 hours and 7 and 14 days after dosing
- Antibody titer (Immunoglobulin G [IgG]) before initiation of an infusion of agalsidase
- Plasma lyso-Gb_3 concentrations and urinary excretion of lyso-Gb_3 before and 14 days after each agalsidase dose

Statistical Methods:

Full details regarding the planned statistical analyses can be found in the final statistical analysis plan (SAP) provided in Appendix 16.1.9. There were 2 subject populations defined for study analyses:

- Safety population: This population included all subjects who received at least 1 dose of agalsidase or migalastat HCl. All safety analyses were performed using the safety population. Subjects were analyzed according to treatment received.
- PK population: This population included all subjects with evaluable PK parameter data, who had successfully completed at least Periods 1 and 2 in any stage. All PK analyses were performed using the PK population.

Plasma migalastat concentrations, plasma α-Gal A activity levels, skin α-Gal A activity levels, WBC α-Gal A activity levels, total α-Gal A protein levels (plasma, skin, urine), urine GL–3 levels, urine lyso-Gb_3 levels, plasma lyso-Gb_3 levels, and plasma IgG titer levels were listed by subject.

NAME OF COMPANY: Amicus Therapeutics, Inc.	INDIVIDUAL STUDY SYNOPSIS	
NAME OF FINISHED PRODUCT: Not Applicable NAME OF ACTIVE INGREDIENT: AT1001 (migalastat hydrochloride)	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(FOR NATIONAL AUTHORITY USE ONLY)

These values and changes from baseline were summarized using descriptive statistics (n, arithmetic mean, standard deviation [SD], coefficient of variation [CV] of the arithmetic mean, geometric mean, CV of the geometric mean, median, minimum, and maximum). Stage 1 and Stage 2 data were presented in separate outputs. In general, within each stage, summaries and mean plots were presented by agalsidase alfa/beta dose level, period, and visit. Individual time profiles were also presented.

PK parameters of AUC_{0-t}, $AUC_{infinity}$, C_{max}, t_{max}, terminal elimination rate constant (K_{el}), and $t_{½}$ were evaluated for plasma migalastat, plasma α-Gal A activity, and plasma total α-Gal A protein. Additionally the percentage of $AUC_{infinity}$ that was extrapolated from t_{last} to infinity ($AUC_{extrapolated}$) was evaluated for plasma total α-Gal A protein. Summary statistics of PK parameters were presented by stage, period, and agalsidase alfa/beta dose and included the arithmetic mean, SD, CV of the arithmetic mean, geometric mean, CV of the geometric mean, median, minimum, and maximum.

The impact of period/treatment in each stage on AUC_{0-t}, $AUC_{infinity}$, and C_{max} of plasma migalastat and agalsidase was assessed based on linear mixed-effects model analyses. The point estimates for geometric means and their associated 90% confidence intervals (CIs) for the test–reference ratios were presented.

Repeated–measures analysis using random-effects models was applied to analyze skin α-Gal A enzyme activity.

All safety parameters were listed by subject. Summaries were presented for incidence of treatment–emergent AEs (TEAEs), related TEAEs, serious TEAEs and serious related TEAEs, TEAEs resulting in study drug being discontinued, TEAEs by maximum severity, and SAEs. The laboratory parameters (hematology and serum chemistry) and vital signs at baseline and each visit, together with changes from baseline at each visit, were summarized using descriptive statistics. Subjects with vital sign values that were outside the potentially clinically significant abnormal (PCSA) ranges at each post-baseline visit were summarized using descriptive statistics. Each urinalysis parameter was summarized at each visit, by frequency counts or descriptive statistics, where appropriate. Shift tables were provided for laboratory parameters (hematology and serum chemistry) and ECG results. A summary of subjects with normal and abnormal physical examination assessment at screening visit was presented by body system.

SUMMARY OF RESULTS

Subject Disposition and Demographics:

Overall, 23 subjects were treated in the study and all subjects completed the study. Twelve subjects were treated in Stage 1 and received 150 mg migalastat HCl, and 11 subjects were treated in Stage 2 and received 450 mg migalastat HCl.

All subjects were males with Fabry disease aged 22-60 years; body mass index (BMI) ranged from 18.4 to 29.2 kg/m^2, and eGFR ranged from 52-140 mL/min/1.73 m^2. All subjects had at least 1 abnormality in the cardiovascular body system; in 21 out of 23 (91.3%) subjects, these

NAME OF COMPANY: Amicus Therapeutics, Inc.	INDIVIDUAL STUDY SYNOPSIS	
NAME OF FINISHED PRODUCT: Not Applicable NAME OF ACTIVE INGREDIENT: AT1001 (migalastat hydrochloride)	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(FOR NATIONAL AUTHORITY USE ONLY)

abnormalities were related to Fabry disease.

Pharmacokinetic and Pharmacodynamic Results:

Primary Endpoints

Effect of Migalastat on Active α-Gal A in Plasma

Single oral doses of 150 mg and 450 mg migalastat HCl co-administered with 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta increased systemic exposures to agalsidase (active plasma α-Gal A AUC levels) by 1.2- to 5.1-fold in 22 out of 23 (95.7%) Fabry subjects relative to agalsidase administered alone. The largest increase (4.1-fold) occurred at the lowest dose of agalsidase (0.2 mg/kg co-administered with 150 mg migalastat HCl), and the smallest increase (2.0-fold) occurred at the highest dose (1.0 mg/kg agalsidase co-administered with either 150 mg or 450 mg migalastat HCl). The overall average relative increase in α-Gal A activity $AUC_{infinity}$ ratio with co-administration of 150 mg migalastat HCl was 2.9-fold and with co-administration of 450 mg migalastat HCl was 2.4-fold. Thus, the magnitude of the increase in the α-Gal A activity was not correlated with migalastat HCl dose.

Effect of Plasma Migalastat on Plasma Total α-Gal A Protein Level

Co-administration of migalastat HCl with 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta had no statistically significant effect on circulating plasma total α-Gal A protein levels. However, for subjects treated with 1.0 mg/kg agalsidase beta, co-administration of migalastat HCl showed a trend of increased total α-Gal A protein in circulation.

Migalastat Plasma Pharmacokinetics

The plasma pharmacokinetics of migalastat were not impacted by co-administration with agalsidase (geometric mean AUC ratio of 150 mg migalastat HCl co-administered with agalsidase to 150 mg migalastat HCl alone = 1.06). The 450 mg dose was approximately dose proportional to the 150 mg dose (geometric mean AUC ratio of 450 mg to 150 mg = 2.57). The single-dose pharmacokinetics of migalastat observed in these Fabry subjects were similar to results from healthy volunteers.

Secondary Endpoint

Effect of Plasma Migalastat on Distribution of Agalsidase to Skin

Following co-administration with 150 mg or 450 mg migalastat HCl, levels of active α-Gal A enzyme in Day 2 skin biopsies demonstrated consistent increases relative to agalsidase alone (19 out of 23 Fabry subjects, 82.6%), verifying proof-of-concept of increased tissue uptake of α-Gal A. Relative to agalsidase alone, increases in active α-Gal A levels in skin following co-administration with migalastat HCl appeared to be migalastat HCl dose-dependent for the 0.2 mg/kg and 0.5 mg/kg agalsidase groups. Relative to baseline, increases in active α-Gal A levels in skin were generally agalsidase dose-dependent.

Exploratory Endpoints

Effect of Plasma Migalastat on Urine GL-3 Concentrations

NAME OF COMPANY: Amicus Therapeutics, Inc.	**INDIVIDUAL STUDY SYNOPSIS**	
NAME OF FINISHED PRODUCT: Not Applicable	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER**	(FOR NATIONAL AUTHORITY USE ONLY)
NAME OF ACTIVE INGREDIENT: AT1001 (migalastat hydrochloride)	**Volume:** **Page:**	

The effect of single oral doses of 150 mg or 450 mg migalastat HCl when co-administered with 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta on urine GL-3 concentrations was not interpretable due to high intra-subject variability. There were no prospective assumptions that treatment effects on urine GL-3 concentrations would be noted in this single-dose study.

Effect of Plasma Migalastat on Distribution of Agalsidase to WBCs

Overall, doses of 150 mg and 450 mg migalastat HCl increased the uptake of active α-Gal A in WBCs; this effect was observed through Day 14 in all agalsidase dose groups. The increase in total α-Gal A protein in WBCs after co-administration of agalsidase with 150 mg or 450 mg migalastat HCl compared to agalsidase alone was observed only through 24 hours, except in 3 subjects who also had increased values at Day 7.

Antibody Titer (IgG)

Of the 23 subjects enrolled into the study, 5 subjects in Stage 1 and 5 subjects in Stage 2 had positive plasma IgG titer levels, with the antibody titers ranging from 12,800 to 819,200. In Stage 1, 4 out of the 5 subjects with positive titers had no change in their titer levels from Day 1 of Period 1 to Day 1 of Period 2; for 1 subject, the titer level decreased from Period 1 to Period 2. In Stage 2, 4 out of the 5 subjects with positive titers had reduced titers in Period 2 compared to Period 1, and 1 subject had the same value on Day 1 of each period. Overall, 4 of the 5 subjects with decreased titer levels from Period 1 to Period 2 had 50% reductions, and 1 subject had a 75% reduction. No subject had an increase in titer values between the 2 study periods.

Effect of Plasma Migalastat on Plasma Lyso-Gb_3 and Urinary Excretion of Lyso-Gb_3

In all treatment groups, the mean plasma lyso-Gb_3 levels across Days 1, 7, and 14 of Periods 1 and 2 were considered to be relatively stable over this timeframe. In all treatment groups except the 150 mg migalastat HCl + agalsidase beta (0.5 mg/kg and 1.0 mg/kg) groups, no relevant differences in mean change from baseline in plasma lyso–Gb_3 across Days 7 and 14 of Periods 1 and 2 or between the 2 periods were observed. In the 150 mg migalastat HCl + agalsidase beta (0.5 mg/kg and 1.0 mg/kg) groups, the results were variable.

In all treatment groups except the 150 mg migalastat HCl + agalsidase beta (0.5 mg/kg and 1.0 mg/kg) groups, the mean urine lyso–Gb_3 levels across Days -1, 1, and 14 of Periods 1 and 2 did not vary by greater than 3-fold and hence were considered to be relatively stable over this timeframe. In the 150 mg migalastat HCl + agalsidase beta (0.5 mg/kg or 1.0 mg/kg) groups, the mean results were variable.

These results suggest that single oral doses of 150 mg or 450 mg migalastat HCl co-administered with 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta to male Fabry subjects showed no relevant or discernible effect on plasma and urine lyso-Gb_3 relative to administration of agalsidase alone. There were no prospective assumptions that treatment effects on plasma and urine lyso-Gb_3 concentrations would be noted in this single-dose study.

Safety Results:

- Overall, during Stage 1 of the study, out of the 12 subjects, a total of 8, 2, and 5 subjects

NAME OF COMPANY: Amicus Therapeutics, Inc.	INDIVIDUAL STUDY SYNOPSIS	
NAME OF FINISHED PRODUCT: Not Applicable NAME OF ACTIVE INGREDIENT: AT1001 (migalastat hydrochloride)	INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER Volume: Page:	(FOR NATIONAL AUTHORITY USE ONLY)

experienced at least 1 TEAE during Periods 1, 2, and 3, respectively. During Stage 2 of the study, out of the 11 subjects, a total of 4 and 5 subjects experienced at least 1 TEAE during Periods 1 and 2, respectively.

- The most commonly reported TEAEs overall were headache (n = 5), diarrhea (n = 3), cardiac murmur (n = 2), nausea (n = 2), peripheral edema (n = 2), paresthesia (n = 2), and dyspnea (n = 2). During Stage 1 of the study, cardiac murmur, peripheral edema, and headache were reported in 2 subjects each; and paresthesia, diarrhea, and dyspnea were reported in 1 subject each. During Stage 2 of the study, headache was reported in 3 subjects, diarrhea and nausea were reported in 2 subjects each, and dyspnea and paresthesia were reported in 1 subject each.
- No treatment-related TEAEs were reported during Stage 1 of the study. During Stage 2 of the study, 2 subjects receiving 0.2 mg/kg agalsidase alfa reported mild, treatment-related TEAEs. One subject experienced treatment-related (treatment not otherwise specified) events of lethargy and nausea in Period 2 (Day 15), and the other subject experienced post-procedural (post-agalsidase injection) hemorrhage in Period 1 (Day 2). All treatment-related events resolved within 3 days with no actions taken.
- There were no deaths or discontinuations of study treatment due to TEAEs reported in this study.
- During the study, 2 SAEs occurred in 1 subject in the 0.5 mg/kg agalsidase beta treatment category: a pre-treatment SAE of transient ischemic attack that resolved 2 days later, before entering Stage 1, Period 1; and a treatment-emergent SAE of Fabry disease-related acute pain and acroparesthesia in Stage 2, Period 1 that resolved the next day. These SAEs were considered unrelated to study treatment.
- Most TEAEs reported during the study were mild in intensity; 6 subjects reported moderate TEAEs (2 in Stage 1, 4 in Stage 2), and 2 subjects reported severe TEAEs (1 in each stage). Both of the severe events (severe paresthesia with onset on Stage 1, Period 1, Day 9; and amaurosis fugax with onset on Stage 2, Period 2, Day 2) were considered non-serious, unlikely related or unrelated to study treatment, and resolved on the same day as onset.
- There were no clinically significant trends noted during the study in the vital signs measurements, physical examinations, laboratory parameters, and ECG recordings.

Conclusions:

- Single oral doses of 150 mg and 450 mg migalastat HCl co-administered with agalsidase increased systemic levels of active α-Gal A by 1.2- to 5.1-fold in 22 out of 23 (95.7%) Fabry subjects relative to agalsidase administered alone over the dose range of 0.2 mg/kg to 1.0 mg/kg.
- Co-administration of migalastat HCl with 0.2 mg/kg agalsidase alfa or 0.5 mg/kg or 1.0 mg/kg agalsidase beta had no statistically significant effect on circulating plasma total α-Gal A protein levels. However, for subjects treated with 1.0 mg/kg agalsidase beta, co-administration of migalastat HCl showed a trend of increased total α-Gal A protein in circulation.

<table>
<tr><td>NAME OF COMPANY:
Amicus Therapeutics, Inc.</td><td colspan="2">INDIVIDUAL STUDY SYNOPSIS</td></tr>
<tr><td>NAME OF FINISHED PRODUCT:
Not Applicable

NAME OF ACTIVE INGREDIENT:
AT1001 (migalastat hydrochloride)</td><td>INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER

Volume:

Page:</td><td>(FOR NATIONAL AUTHORITY USE ONLY)</td></tr>
<tr><td colspan="3">• Plasma migalastat exposures were not affected by co-administration with agalsidase alfa (0.2 mg/kg) or agalsidase beta (0.5 mg/kg and 1.0 mg/kg).
• Co-administration of migalastat HCl with agalsidase increased the levels of active α-Gal A in Day 2 skin biopsies in 19 out of 23 (82.6%) Fabry subjects over the dose range of 0.2 mg/kg to 1.0 mg/kg. This effect was migalastat dose-dependent for the 0.2 mg/kg and 0.5 mg/kg agalsidase groups. Increases in active α-Gal A levels in skin were generally agalsidase dose-dependent.
• Co-administration of migalastat HCl at doses of 150 mg and 450 mg with agalsidase was generally well-tolerated.</td></tr>
<tr><td colspan="3">Date of Final Report: 12 September 2014</td></tr>
</table>