2. SYNOPSIS

Name of Sponsor/Company: Amicus Therapeutics, Inc.	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Finished Product: N/A		
Name of Active Ingredient: Duvoglustat		

Title of Study: An open-label, multicenter study to evaluate the safety, tolerability, pharmacodynamics, and pharmacokinetics of three dosing regimens of oral AT2220 in patients with Pompe disease

Investigators: [redacted]

Study center:
There was one site that enrolled subjects into this study:

Site 07: [redacted]

Publications (reference): None as of the date of this report.

Studied period: Date first patient enrolled: 08 December 2008 Date last patient completed: 14 December 2009	**Phase of development:** 2

Methodology:
This was a Phase 2, multicenter study to evaluate the safety, efficacy, tolerability, pharmacodynamics, and pharmacokinetics of three dosing regimens of oral duvoglustat. This study consisted of a 28-day screening period, an 11-week treatment period, and a 1-week follow-up period. The three dosing cohorts were as follows: Cohort 1: duvoglustat HCl, 2.5 g daily for 3 days, followed by no study drug for 4 days; Cohort 2: duvoglustat HCl, 5 g daily for 3 days, followed by no study drug for 4 days; Cohort 3: duvoglustat HCl, 5 g daily for 7 days, followed by no study drug for 7 days. Subjects could participate in only 1 cohort. The first 6 subjects were to be enrolled in cohort 1, followed by a safety review after the last subject had completed 3 weeks of dosing to determine if enrollment into Cohorts 2 and 3 will proceed.

Number of patients (planned and analyzed): Approximately 18 subjects were planned (6 subjects per cohort); three subjects enrolled.

Eligibility Criteria: To participate in this study, subjects must have a diagnosis of Pompe disease, be 18-74 years of age (inclusive), and be naïve to ERT with rhGAA or have not

received rhGAA within the 3 months prior to screening. For complete lists of all inclusion and exclusion criteria, refer to the protocol (provided in Appendix 16.1.1).

Test product, dose and mode of administration, batch number:
Duvoglustat HCl, doses of 2.5 g administered orally.

The batch number for study drug used was: PT-C05082642-E06005.

Duration of treatment: The planned duration of treatment, for an individual subject, was 11 weeks.

Reference therapy, dose and mode of administration, batch number: Not applicable

Criteria for evaluation: Safety was evaluated by changes in physical examinations and vital signs (blood pressure, heart rate, and respiratory rate), treatment-emergent safety laboratory assessments (hematology, chemistry, and urinalysis), electrocardiogram (ECG) abnormalities, adverse events (AEs), and changes in concomitant medications.

Safety Results:
The three subjects enrolled into this study discontinued after completion of Visit 3. Two subjects were discontinued from the study due to serious adverse events (SAEs) of muscle weakness and TEAEs of increased creatine phosphokinase (CK). The third subject was withdrawn at the discretion of the investigator. All three subjects experienced TEAEs of increased muscle weakness, and similar increases in laboratory values of alanine aminotransferase (ALT), aspartate aminotransferase (AST), CK, lactate dehydrogenase (LDH), and aldolase, all of which were deemed possibly or probably related to study drug and were moderate to severe in intensity. Subjects [redacted] and [redacted] experienced TEAEs of falls which were reported as possibly related to study drug. In all three subjects, the TEAEs and increased laboratory values were of prolonged duration with a gradual improvement following discontinuation of study drug.

Conclusion:
A persistent high concentration of duvoglustat in muscle tissue likely explains the adverse findings in this study. This appeared to exacerbate the subjects' pre-existing pathophysiology. Subjects with Pompe disease, as compared to healthy subjects, experience prolonged GAA suppression at the site of action, due to lower baseline GAA activity. The prolonged duration of these effects are likely attributable to the length of time that duvoglustat remains in skeletal muscle tissue, as demonstrated in separate studies.

Date of the original report: 26 July 2013

Date of Amendment 1: 29 October 2013