ATH-1017-AD-0203 OLEX Analysis Summary

Sponsor:	Athira Pharma, Inc.
Sponsor Address:	18706 North Creek Parkway Suite 104 Bothell, WA 98011
Protocol Number:	ATH-1017-AD-0203 Open Label Extension Study
Study Title	Open-Label Extension of Studies ATH-1017-AD-0201 and ATH-1017-AD-0202 in Subjects with Mild to Moderate Alzheimer's Disease
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Confidentiality Statement

Approvals

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Document History - Changes Compared to Previous Version

Version	Date	Changes
1.0	02Oct2024	Initial Version
1.1	05Dec2024	Added 4 Listings, 1 Figure and updated footnotes for some outputs to note participants might be counted for both dose groups.

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ABBREVIATIONS

AE	Adverse Event
AD	Alzheimer's Disease
ApoE	Apolipoprotein E
ERP	Event related potential
FDA	Food and Drug Administration
FPI	First Patient In
FTP	File Transfer Protocol
GCP	Good Clinical Practice
MMSE	Mini-Mental State Examination
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SPO	Share Point Online
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TLFs	Tables, Listings, and Figures

1 INTRODUCTION AND SCOPE

The purpose of this Analysis Summary is to describe the framework for the reporting, summarization and statistical analysis methodology of the safety parameters measured throughout the study. [redacted]

As the study was terminated by the Sponsor, only a basic set of safety tables, listings and figures will be generated.

As per the protocol, the baseline flag will be assigned to the Visit 8 assessment from parent study for the participants who entered in OLEX without the time gap and then to the Rollover Visit 2 Day 1 assessment from the OLEX study for the subject who entered in OLEX with Gap >= 30 days.

If Visit 8 and Visit 9 records are missing in the parent study for a participant, the baseline value will be considered missing. Therefore, those specific participants will be excluded from change from baseline calculations.

Due to strict database lock timelines, any minor updates to TLF shells post-signature will not require a new version of this Analysis Plan.

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Output Type/Number	**Title**
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Figure 14.3.1.1	eDISH (evaluation of Drug Induced Serious Hepatotoxicity)

3 TLF DRY RUN APPROACH

No formal Dry Run is or will be scheduled prior to database lock. Once database lock occurs, the TLFs specified in the Table of Contents and Attachment A will be refreshed. MMS will internally review the TLFs prior to delivery to Athira. Once the TLFs and datasets are delivered to Athira, they will be considered Post-DBL Draft 1. Athira will have an opportunity to comment and make slight adjustments via the comment log on the SharePoint site. A Comment Resolution Meeting (CRM) will be scheduled between the main points of contact from both parties, if needed. MMS will consider all comments and will update the TLFs accordingly. Changes to the approved TLF specifications, requests for additional/new outputs, and/or programmatic updates to resolve data issues will incur additional cost and may impact the timeline. The next delivery of TLFs / datasets will be considered Final.

ATTACHMENT A – TLF SPECIFICATIONS

ICH E3 TLG NUMBERING GUIDELINE

- **Guideline for Industry: Structure and Content of Clinical Study Reports**
  This is a summary of the guideline as it applies to numbering tables, listings and graphs for programmers and statisticians. To ensure most current guideline is being followed, reference the link on fda.gov.
  https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073113.pdf

- **Section 14.x TABLES, FIGURES, AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT**
  - 14.1 Demographic Data Summary figures and tables
  - 14.2 Efficacy Data Summary figures and tables
  - 14.3 Safety Data Summary figures and tables
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- **Section 16.x APPENDICES**
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    - 16.2.7 Adverse event listings (each patient)
    - 16.2.8 Listing of individual laboratory measurements by patient, when required by regulatory authorities
  - 16.3. Case Report Forms (CRF's)
    - 16.3.1 CRF's for deaths, other serious adverse events, and withdrawals for adverse events
    - 16.3.2 Other CRF's submitted
  - 16.4 Individual Patient Data Listings

- If there are multiple listings that belong in one of the ICH appendix sections, the number format should be 16.2.X.Y. (X=ICH number listed above, Y = sequential number). Example, if there are 5 AE listings then they would be number 16.2.7.1 to 16.2.7.5. If there is only one, then use 16.2.7.

DISPOSITION, DEMOGRAPHICS, AND BASELINE CHARACTERISTICS

Table 14.1.1.4
Participant Disposition, Early Withdrawal from the Study
Safety Population

Disposition/ Reason	40 mg ATH-1017 n (%)	70 mg ATH-1017 n (%)	Overall n (%)
Safety population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ongoing Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary reason for discontinuation of the study - n (%)			
Any Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lack of Efficacy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Subject or Legally Authorized Representative (LAR)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)
Non-Compliance with Study Drug	xx (xx.x)	xx (xx.x)	xx (xx.x)
Site Terminated by Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)
Repeat incapacity of subject and/or caregiver (in the judgement of the investigator to properly administer drug)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Prolonged or definitive loss of caregiver without adequate replacement	xx (xx.x)	xx (xx.x)	xx (xx.x)
Nursing home replacement	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
Week of Early Withdrawal			
0-2 Weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
2-4 Weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
…	xx (xx.x)	xx (xx.x)	xx (xx.x)
32-34 Weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
MISSING END OF STUDY DATE	xx (xx.x)	xx (xx.x)	xx (xx.x)

- Percentages are calculated using the number of participants in each treatment group as the denominator.
- Participants receiving both 40 mg and 70 mg are counted in both dose groups; Overall is not a summation of the dose groups.

NOTE: Ensure that the primary reason for discontinuation of study listed in the shell matches the options in the CRF.

Programming Notes:

- Week of Early Withdrawal displayed in the interval of 2 weeks till last available week data.

Table 14.1.1.5
Major Protocol Deviations
Safety Population

Major Protocol Deviation/ Reasons	40 mg ATH-1017 (N=xxx) n(%)	70 mg ATH-1017 (N=xxx) n(%)	Overall (N=xxx) n(%)
Number of participants with at least 1 major protocol deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)
Inclusion/Exclusion Criteria	xx (xx.x)	xx (xx.x)	xx (xx.x)
Informed Consent Procedures	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Procedures	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit Schedule/Interval	xx (xx.x)	xx (xx.x)	xx (xx.x)

- A participant with multiple protocol deviations within a deviation category or deviation term is counted only once.
- Participants may have multiple protocol deviations.
- Participants with a reported major protocol deviation in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported a major protocol deviation during the 40mg timeframe, that new major protocol deviation is reported in the 40mg column. If the same major protocol deviation reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.
- If deviation start date is missing, the deviation is counted in each dose groups.

Programming Notes:

- Please add all the possible major protocol reasons as per the data collected.

Table 14.1.2.1
Demographics and Baseline Characteristics
Safety Population

Parameter Statistic	40 mg ATH-1017 (N=xxx)		70 mg ATH-1017 (N=xxx)	Overall (N=xxx)
Age at Informed Consent (years)				
n	xxx		xxx	xxx
Mean (SD)	xx.x (x.xx)		xx.x (x.xx)	xx.x (x.xx)
Median	xx.x		xx.x	xx.x
(Q1, Q3)	(xx.x, xx.x)		(xx.x, xx.x)	(xx.x, xx.x)
Min, Max	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
P-value		x.xxxx		
Age Group - n(%)				
<65 years	xx (xx.x)		xx (xx.x)	xx (xx.x)
>= 65 years	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Available	xx (xx.x)		xx (xx.x)	xx (xx.x)
P-value		x.xxxx		
Ethnicity - n(%)				
Hispanic Or Latino	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Hispanic Or Latino	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Specified	xx (xx.x)		xx (xx.x)	xx (xx.x)
Unknown	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Available	xx (xx.x)		xx (xx.x)	xx (xx.x)
P-value		x.xxxx		
Race - n(%)				
American or Alaskan Native	xx (xx.x)		xx (xx.x)	xx (xx.x)
Asian	xx (xx.x)		xx (xx.x)	xx (xx.x)
Black	xx (xx.x)		xx (xx.x)	xx (xx.x)
Hawaiian or Pacific Islander	xx (xx.x)		xx (xx.x)	xx (xx.x)
White	xx (xx.x)		xx (xx.x)	xx (xx.x)
Other	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Available	xx (xx.x)		xx (xx.x)	xx (xx.x)
American or Alaskan Native	xx (xx.x)		xx (xx.x)	xx (xx.x)
P-value		x.xxxx		
Sex - n(%)				
Male	xx (xx.x)		xx (xx.x)	xx (xx.x)
Female	xx (xx.x)		xx (xx.x)	xx (xx.x)
Not Available				
P-value		x.xxxx		

Parameter Statistic	40 mg ATH-1017 (N=xxx)		70 mg ATH-1017 (N=xxx)	Overall (N=xxx)
Years of Education				
n	xxx		xxx	xxx
Mean (SD)	xx.x (x.xx)		xx.x (x.xx)	xx.x (x.xx)
Median	xx.x		xx.x	xx.x
(Q1, Q3)	(xx.x, xx.x)		(xx.x, xx.x)	(xx.x, xx.x)
Min, Max	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
P-value		x.xxxx		
Height (cm)				
n	xxx		xxx	xxx
Mean (SD)	xx.x (x.xx)		xx.x (x.xx)	xx.x (x.xx)
Median	xx.x		xx.x	xx.x
(Q1, Q3)	(xx.x, xx.x)		(xx.x, xx.x)	(xx.x, xx.x)
Min, Max	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
P-value		x.xxxx		
Weight (kg)				
n	xxx		xxx	xxx
Mean (SD)	xx.x (x.xx)		xx.x (x.xx)	xx.x (x.xx)
Median	xx.x		xx.x	xx.x
(Q1, Q3)	(xx.x, xx.x)		(xx.x, xx.x)	(xx.x, xx.x)
Min, Max	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
P-value		x.xxxx		
Body Mass Index (kg/m^2)				
n	xxx		xxx	xxx
Mean (SD)	xx.x (x.xx)		xx.x (x.xx)	xx.x (x.xx)
Median	xx.x		xx.x	xx.x
(Q1, Q3)	(xx.x, xx.x)		(xx.x, xx.x)	(xx.x, xx.x)
Min, Max	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
P-value		x.xxxx		

- SD: Standard Deviation, Q1: 1st Quartile, Q3: 3rd Quartile; n: number of participants with values for given treatment group.
- Percentages are calculated using the number of participants in each treatment group as the denominator.
- MMSE Severity = Mild if MMSE total Score is between 20-24. MMSE Severity = Moderate if MMSE total Score is between 14-19.
- p-values presented test for a difference between participants who received 40mg ATH-1017 and participants who received 40mg ATH-1017. A 2 sample t-test is used to test the difference for continuous variables and a chi-squared test of independence is used to test the difference for categorical variables. N: number of Participants in the specified population without Acetylcholinesterase Inhibitors for given treatment group. Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Exposure

Table 14.1.4.1
Duration of Exposure to Study Treatment
Safety Population

Category	40 mg ATH-1017 (N=xxx)	70 mg ATH-1017 (N=xxx)	Overall (N=xxx)
Duration of study treatment (days)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx
Min	xx	xx	xx
Median	xx.x	xx.x	xx.x
Q1,Q3	xx,xx	xx,xx	xx,xx
Max	xx	xx	xx
Duration of exposure, n(%)			
At least 1 dose	xx (xx.x)	xx (xx.x)	xx (xx.x)
2 days to <4 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
4 weeks to <8 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
8 weeks to <12 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
12 weeks to <16 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
16 weeks to <20 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
20 weeks to <24 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
24 weeks to <48 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
48 weeks to <72 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
72 weeks to <96 weeks	xx (xx.x)	xx (xx.x)	xx (xx.x)
96 weeks or more	xx (xx.x)	xx (xx.x)	xx (xx.x)

- SD: Standard Deviation, Q1: 1st Quartile, Q3: 3rd Quartile
- Day is relative to first dose date.
- Duration of Exposure (Days) defined as date of last dose - date of first dose +1
- Participants receiving both 40 mg and 70 mg are counted in both dose groups for their respective time in each dose group; Overall is not a summation of the dose groups.

Programming Notes:

- Duration of Exposure (Days) defined as date of last dose - date of first dose +1. For participants ongoing at time of the data cut, the date of cut-off was used as the date of last dose.

SAFETY DATA

Displays of Adverse Events

Table 14.3.1.1
Overall Summary of Adverse Events
Safety Population

	40 mg ATH-1017 (N=xxx) n(%)	70 mg ATH-1017 (N=xxx) n(%)	Overall (N=xxx) n(%)
Number of participants with at least 1 AE	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of participants with at least 1 TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of participants with at least 1 Treatment-Related TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)
Participants with serious or other significant TEAEs			
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)
SAE(s)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treatment-Related Serious TEAE(s)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs Leading to Study Drug Withdrawal	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs Leading to Study Drug Interruption	xx (xx.x)	xx (xx.x)	xx (xx.x)
TEAEs Leading to Study Withdrawal	xx (xx.x)	xx (xx.x)	xx (xx.x)

- AE: Adverse Event; TEAE: Treatment Emergent Adverse Event; SAE: Serious Adverse Event. N: number of Participants in the specified population for given treatment group. Related includes related, probably related, and possibly related events.
- Percentages are based on the Safety Population; Deaths are AEs with reported outcome of Fatal.
- All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.
- Participants with a reported AE in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an AE during the 40mg timeframe, that new AE is reported in the 40mg column. If the same event reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

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Programming Notes:

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Table 14.3.1.2
Treatment Emergent Adverse Events by Primary System Organ Class and Preferred Term
Safety Population

System Organ Class (SOC) Preferred Term (PT)	40 mg ATH-1017 (N=xxx) n (%)	70 mg ATH-1017 (N=xxx) n (%)	Overall (N=xxx) n (%)
Number of participants with at least 1 TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)

- TEAE: Treatment Emergent Adverse Event; n = number of participants with at least one TEAE occurring; % = (n/N) *100; N: number of participants in the specified population for given treatment group. Percentages based on Safety Population. SOCs are presented alphabetically; PTs are sorted by decreasing frequency in the Overall column. A participant with multiple adverse events within a primary SOC and PT is counted only once for raw incidence rates. All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0. Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received. Participants with a reported AE in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an AE during the 40mg timeframe, that new AE is reported in the 40mg column. If the same event reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

Table 14.3.1.3
Treatment-Related TEAEs by Primary System Organ Class and Preferred Term
Safety Population

Repeat Table 14.3.1.2 for Treatment-Related TEAEs.
Replace first row with “Number of participants with at least 1 Treatment-Related TEAE”

Programming Notes: Add below footnote additionally
- Related includes related, probably related, and possibly related events.

Table 14.3.1.4
Serious TEAEs by Primary System Organ Class and Preferred Term
Safety Population

Use the Table 14.3.1.2 shell.
Replace first row with "Number of participants with at least 1 Serious TEAE"
NOTE: subset this table to show Serious TEAEs.

Programming Notes:

Table 14.3.1.5
Treatment-Related Serious TEAEs by Primary System Organ Class and Preferred Term
Safety Population

Use the Table 14.3.1.2 shell.
Replace first row with "Number of participants with at least 1 Treatment-Related Serious TEAE"
NOTE: subset this table to show Treatment-Related Serious TEAEs.

Programming Notes: Add below footnote additionally
- Related includes related, probably related, and possibly related events.

Table 14.3.1.6
Adverse Events Leading to Study Drug Withdrawal by Primary System Organ Class and Preferred Term
Safety Population

Use the Table 14.3.1.2 shell.
Replace first row with "Number of participants with at least 1 AE leading to study drug withdrawal"
NOTE: subset this table to show AEs leading to study drug discontinuation only.

Programming Notes:

-

Table 14.3.1.7
Adverse Events Leading to Study Drug Interruption by Primary System Organ Class and Preferred Term
Safety Population

Use the Table 14.3.1.2 shell.
Replace first row with "Number of participants with at least 1 AE leading to study drug interruption"

NOTE: subset this table to show AEs leading to study drug interruption only.

Programming Notes:

-

Table 14.3.1.8
Treatment Emergent Adverse Events by Primary System Organ Class, Preferred Term, and Maximum Severity
Safety Population

Primary System Organ Class (SOC)/ Preferred Term (PT)	Severity	40 mg ATH-1017 (N=xxx) n(%)	70 mg ATH-1017 (N=xxx) n(%)	Overall (N=xxx) n(%)
Number of participants with at least 1 TEAE	Overall	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
System organ class 1	Overall	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	Overall	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	Overall	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)

- TEAE: Treatment Emergent Adverse Event. A participant with multiple adverse events within a SOC or PT and a given severity is counted only once
n = number of participants with at least one TEAE occurring; % = (n/N) *100. N: number of participants in the specified population for given treatment group. Percentages are based on the Safety Population. SOCs are presented alphabetically; PTs are sorted within SOC in descending frequency in the 40mg ATH-1017 column. All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0. Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received. Participants with a reported AE in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an AE during the 40mg timeframe, that new AE is reported in the 40mg column. If the same event reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

Table 14.3.1.9
Injection Site Reactions by Preferred Term
Safety Population

Preferred Term (PT)	40 mg ATH-1017 (N=xxx) n (%)	70 mg ATH-1017 (N=xxx) n (%)	Overall (N=xxx) n (%)
Number of participants with at least 1 ISR TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)

- ISR = Injection site reaction; TEAE = treatment-emergent adverse event;
- n = number of participants with at least one TEAE occurring; % = (n/N) *100;
- N: number of participants in the specified population for given treatment group.
- All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0.
- Participants with a reported ISR in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an ISR during the 40mg timeframe, that new ISR is reported in the 40mg column. If the same ISR reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

Programming Notes:

- Table should be sorted by the descending frequency of the ISR PT in the Overall column.

Listings of Deaths, Other Serious and Significant Adverse Events

Listing 14.3.2.1
Deaths Reported
Safety Population

Treatment	Participant ID	TEAE	Relationship to IMP	AChEI Usage/Age/Sex/ Race	Start Date/Time of Study Treatment (Day)	Last Date/Time of Study Treatment (Day)	Death Date/Time (Day)	Reason for Death/ Preferred Term
XXXXXXXXX	xxxxxxxx	Y	xxxxxx	Y/xx/M/ xx	YYYY-MM-DD HH:MM (xx)	YYYY-MM-DD HH:MM (xx)	YYYY-MM-DDT HH:MM (xx)	xxxxxxxxx/ xxxxxxxx
XXXXXXXXX	xxxxxxxx	N	xxxxxx	N/xx/F/ xx	YYYY-MM-DD HH:MM (xx)	YYYY-MM-DD HH:MM (xx)	YYYY-MM-DDT HH:MM (xx)	xxxxxxxxx/ xxxxxxxx

- AChEI: Acetylcholinesterase inhibitor; M: Male; F: Female; IMP: Investigational Medicinal Product;
- Day is relative to the date of first drug administration.
- Missing dates are based on imputed dates (see SAP Appendix 4 for details).
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Programming Notes:

-

Listing 14.3.2.2
Serious Adverse Events
Safety Population

Treatment	Participant ID	AChEI Usage/Age/ Sex/ Race	System Organ Class (SOC)/ Preferred Term (PT)/ Reported Term	Start Date (Day)/ End Date (Day) or Ongoing	TEAE	Severity	Treatment Given for AE/ Relationship to IMP/ Relationship to Study Procedure/ Action Taken/ Outcome
XXXXXXXX	xxxxxxxx	Y/xx/ M/ xx	xxxx/ xxxx/ xxxx	YYYY-MM-DD HH:MM (xx)/ YYYY-MM-DD HH:MM(xx)	Y	MILD	Y/ Related/ Related/ Dose not changed/ Recovered/resolved N/ Unrelated/ Related/ Dose not changed/ Recovered/resolved
XXXXXXXX	xxxxxxxx	N/xx/ F/ xx	xxxx/ xxxx/ xxxx	YYYY-MM-DD HH:MM (xx)/ YYYY-MM-DD HH:MM (xx)	N	MOD	Treatment Given for AE/ Relationship to IMP/ Relationship to Study Procedure/ Action Taken/ Outcome

- TEAE: Treatment Emergent Adverse Event; IMP: Investigational Medicinal Product; AChEI: Acetylcholinesterase inhibitor; M: Male; F: Female.
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- Day is relative to the date of first drug administration.
- All AE terms were coded to Medical Dictionary for Regulatory Activities Terminology (MedDRA®) version 24.0.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

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Programming Notes:

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Listing 14.3.2.3
Adverse Events
Safety Population

Use the Listing 14.3.2.2 shell

Programming Notes: Repeat for AEs

-

Laboratory Results

Consider the following decimal precision as a guide for the mean for each parameter, if reported in SI units.

Parameter	Decimal Precision for Mean
Hematology: Hemoglobin, platelets **Chemistry**: sodium, chloride, bicarbonate, creatinine, protein, albumin, ALT, AST, GGT, ALP, CK, LDH	1
Hematology: erythrocytes, leukocytes, lymphocytes, neutrophils, basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes, neutrophils/leukocytes **Chemistry**: potassium, glucose (fasting and non-fasting), urea nitrogen, total bilirubin (total, direct, indirect), triglycerides, cholesterol (total, LDL, HDL) **Coagulation**: prothrombin time, INR, APTT	2
Hematology: Hematocrit, basophils, eosinophils, monocytes **Chemistry**: calcium, phosphate	3

Note:

- SD = mean + 1,
- Median = mean
- Min/Max = mean – 1

Chemistry results are usually displayed in alphabetical order. For hematology results, the following order is suggested:

- HGB, HCT, WBC, BASO, EOS, LYM, MONO, NEUT, BASOLE, EOSLE, LYMLE, MONOLE, NEUTLE, RBC, PLAT.

Table 14.3.4.3
Shift from Baseline to Post-Baseline Visits and Worst Post-Baseline Visit in Hematology Values
Safety Population

Parameter: xxxx (units) (Low:<xxx/High:>xxx), (Low:<xxx/High:>xxx), (Low:<xxx/High:>xxx), (Low:<xxx/High:>xxx)

		Worst Value During Study							
	Baseline	Low		Normal		High		Overall	
Treatment	Grade	n	(%)	n	(%)	n	(%)	n	(%)
Overall (N=xxx)	Low	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
	Normal	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
	High	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
	Total	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)

- n: the number of participants who have values at both baseline (normal and abnormal) and post-baseline (abnormal).
- Baseline is defined as the last measurement prior to first dose.
- Overall column is the number of unique participants that have non-missing baseline values.
- Percentage for each grade is calculated using the number of participants in the Overall column.
- If a participant had a post-baseline value equal to LOW and another equal to HIGH, the participant is counted in each respective column.
- Low / Normal / High thresholds are based on the lower and upper limits of normal.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

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Programming Notes:

- Replace highlighted Low/High with given low/high for parameter.
- For the subtitle of Parameter and the low/high values, if there are multiple reference ranges for a specific parameter, please display all range pairs.

NOTE:

- Worst value should be defined in the Protocol as low, high, or both or sponsor can confirm.
- If the missing category is not needed, then it can be omitted if a footnote is added specifying that only the participants with non-missing baseline and at least 1 non-missing post-baseline are included. This table can be repeated for specific time points instead of "worst value during study".

Programming Notes:

- Please add missing rows or columns as per data requirements for completeness.
- The Visits will be displayed and also Worst Post-Baseline Visit - <High/Low> assessment also displayed here.
- Please sort in this order: HGB, HCT, WBC, BASO, EOS, LYM, MONO, BASOLE, EOSLE, LYMLE, MONOLE, NEUTLE, RBC, PLAT.

Table 14.3.4.6
Shift from Baseline to Post-Baseline Visits and Worst Post-Baseline Visit in Chemistry Values
Safety Population

Use the Table 14.3.4.3 shell.
NOTE: subset this table to show Chemistry lab parameters.

Programming Notes:

Table 14.3.4.9A
Shift from Baseline to Post-Baseline Visits in Urinalysis Values (Normal/Abnormal)

Safety Population

Use the Table 14.3.4.3 shell.
NOTE: subset this table to show Urinalysis lab parameters.

Table 14.3.4.9B
Shift from Baseline to Post-Baseline Visits and Worst Post-Baseline Visit in Urinalysis Values (Low/Normal/High)
Safety Population

Use the Table 14.3.4.3 shell.
NOTE: subset this table to show Urinalysis lab parameters.

Programming Notes:

Table 14.3.7.9
Summary of Liver Related Laboratory Abnormalities
Safety Population

Parameter/Potentially Clinically Significant Criterion	40 mg ATH-1017 (N=xxx) N1	40 mg ATH-1017 (N=xxx) n (%)	70 mg ATH-1017 (N=xxx) N1	70 mg ATH-1017 (N=xxx) n (%)	Overall (N=xxx) N1	Overall (N=xxx) n (%)
Alanine Aminotransferase	xx		xx		xx	
<LLN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Normal (>=LLN - <=ULN)		xx (xx.x)		xx (xx.x)		xx (xx.x)
>1 - 3 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>3 - 5 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>5 - 10 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>10 - 20 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>20 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Aspartate Aminotransferase	xx		xx		xx	
<LLN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Normal (>=LLN - <=ULN)		xx (xx.x)		xx (xx.x)		xx (xx.x)
>1 - 3 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>3 - 5 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>5 - 10 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>10 - 20 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>20 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Alkaline Phosphatase	xx		xx		xx	
<LLN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Normal (>=LLN - <=ULN)		xx (xx.x)		xx (xx.x)		xx (xx.x)
>1 - 2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
>2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Bilirubin	xx		xx		xx	
<LLN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Normal (>=LLN - <=2 x ULN)		xx (xx.x)		xx (xx.x)		xx (xx.x)
>2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
Hy's Law: ALT/AST>=3 x ULN and BILI>=2xULN	xx		xx		xx	
Criteria Not Met		xx (xx.x)		xx (xx.x)		xx (xx.x)
With ALP <2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
With ALP >=2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)
ALP >=2 x ULN	xx		xx		xx	
Criteria Not Met		xx (xx.x)		xx (xx.x)		xx (xx.x)
With ALT/AST <2 x ULN		xx (xx.x)		xx (xx.x)		xx (xx.x)

With ALT/AST >=2 x ULN	xx (xx.x)	xx (xx.x)	xx (xx.x)

- ULN: Upper Limit of Normal; LLN: Lower Limit of Normal. n = the number of participants with at least once post-baseline for the corresponding parameter. N1 = the number of participants who had at least 1 post-baseline assessment for the corresponding parameter; Percentages are based on N1. N: number of participants in the specified population for given treatment group.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received. Participants with an abnormality in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an abnormality during the 40mg timeframe, that new abnormality is reported in the 40mg column. If the same abnormality reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.
- Lab ranges between 201 and 203 differ due to differing lab vendors used.

Programming notes:

Table 14.3.7.11
Summary of Eosinophil Lab Abnormalities
Safety Population

Parameter PCS Criterion	40mg ATH-1017 (N=xxx) N1	n (%)	70mg ATH-1017 (N=xxx) N1	n (%)	Overall (N=xxx) N1	n (%)
Eosinophilia	xx		xx		xx	
Eosinophils >= 1500/uL		xx (xx.x)		xx (xx.x)		xx (xx.x)
Eosinophils >= 3000/uL		xx (xx.x)		xx (xx.x)		xx (xx.x)
Eosinophils >= 5000/uL		xx (xx.x)		xx (xx.x)		xx (xx.x)

- PCS: potentially clinically significant.
- n = the number of participants that met PCS criteria at least once post-baseline for the corresponding parameter.
- N1 = the number of participants who had at least 1 post-baseline assessment for the corresponding parameter; Percentages are based on N1.
- N: number of participants in the specified population for given treatment group.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.
- Participants with an abnormality in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported an abnormality during the 40mg timeframe, that new abnormality is reported in the 40mg column. If the same abnormality reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

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Programming Notes:

- Split pages after 70mg group if doesn’t fit

Vital Signs

Table 14.3.6.2
Potential Vital Signs Values of Concern at Any Time Post-Baseline
Safety Population

Vital Sign Abnormal Category	40 mg ATH-1017 (N=xxx)		70 mg ATH-1017 (N=xxx)		Overall (N=xxx)	
	N1	n(%)	N1	n(%)	N1	n(%)
Orthostatic Diastolic BP (mmHg)	xx		xx		xx	
Standing Diastolic BP Decrease >=10mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Diastolic BP Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Diastolic BP >100mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Diastolic BP >100 and Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Diastolic BP <50 and Decrease >=10mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Diastolic BP <50mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Orthostatic Systolic BP (mmHg)	xx		xx		xx	
Standing Systolic BP Decrease >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Systolic BP Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Systolic BP >160mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Standing Systolic BP >160 and Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Systolic Blood Pressure (mmHg)						
Systolic BP Decrease >=20mmHg	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)
Systolic BP Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Systolic BP >160mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Systolic BP >160 and Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Diastolic Blood Pressure (mmHg)						
Diastolic BP Decrease >=10mmHg	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)
Diastolic BP Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Diastolic BP >100 and Increase >=20mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Diastolic BP <50 and Decrease >=10mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Diastolic BP >100mmHg		xx (xx.x)		xx (xx.x)		xx (xx.x)
Pulse Rate (beats/min)	xx		xx		xx	
Abnormal Heart Rate (<50 or >100 BPM)		xx (xx.x)		xx (xx.x)		xx (xx.x)
Heart Rate Change >= 30 BPM		xx (xx.x)		xx (xx.x)		xx (xx.x)

- N1: the number of participants who have values at both baseline and post-baseline.
- Percentages are based on the Safety population. Participants may fall into more than one category.
- Participants with a potential value of concern in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported a potential value of concern during the 40mg timeframe, that new potential value of concern is reported in the 40mg column. If the same potential value of concern reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

Programming Notes:

- Visit can be added as a column to the left, if requested

ECG Tables

Table 14.3.7.4
ECG Interpretation at Any Time Post-Baseline
Safety Population

Parameter Finding	40 mg ATH-1017 (N=xxx) n(%)	70 mg ATH-1017 (N=xxx) n(%)	Overall (N=xxx) n(%)
Interpretation – N1	xxx	xxx	xxx
Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)
Abnormal	xx (xx.x)	xx (xx.x)	xx (xx.x)

- N1: the number of participants who have values at both baseline and post-baseline.
- N: number of participants in the specified population for given treatment group.
- Percentages are based on N1.
- A participant is counted only once for each finding category they fall into; if a participant has at least 1 abnormal record it is counted in the abnormal category.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.
- Participants with an interpretation in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported a interpretation during the 40mg timeframe, that new interpretation is reported in the 40mg column. If the same interpretation reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

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Programming Notes:

- Any abnormal finding for any post baseline visit will be counted as Abnormal.

Table 14.3.7.5
Shift from Baseline to Post-Baseline Visits in ECG Values
Safety Population

Use the Table 14.3.4.3 shell.
NOTE: This table to show ECG parameters.

Programming Notes:

- Please add missing rows as per data requirements for completeness.
- Use "Visit (Timepoint)" concatenated in place of 'Visit" used in the Table 14.3.4.9A. The Visits will be displayed and also Worst Post-Baseline (Abnormal any time Post-Baseline) visit assessment also displayed here.

Table 14.3.7.6
Potential ECG Values of Concern at Any Time Post-Baseline
Safety Population

ECG Parameter Abnormal Category	40 mg ATH-1017 (N=xxx)		70 mg ATH-1017 (N=xxx)		Overall (N=xxx)	
	N1	n(%)	N1	n(%)	N1	n(%)
ECG Mean Heart Rate	xx		xx		xx	
Heart Rate < 50 bpm		xx (xx.x)		xx (xx.x)		xx (xx.x)
QRS Duration, Aggregate	xx		xx		xx	
QRS Duration > 120 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QRSAG Change > 25 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
PR Interval, Aggregate	xx		xx		xx	
PR Interval > 250 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
PRAG Change > 50 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcB Interval, Aggregate	xx		xx		xx	
QTcB Value >= 500 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcB Change >= 60 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcB Value >= 500 and Change >= 60 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcF Interval, Aggregate	xx		xx		xx	
QTcF Value >= 500 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcF Change >= 60 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)
QTcF Value >= 500 and Change >= 60 msec		xx (xx.x)		xx (xx.x)		xx (xx.x)

- ECG: Electrocardiogram; QRS: Quantronic Resonance System: PR: P-wave to QRS complex; QTcB: Heart rate-corrected QT Interval; QTcF: QT Interval Corrected using Fridericia's Formula; QRSAG: QRS Aggregate; N1: the number of participants who have values at both baseline and post-baseline.
- N: number of participants in the specified population for given treatment group. Percentages are based on N1. Participants may fall into more than one category. Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received. Participants with a potential value of concern in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported a potential value of concern during the 40mg timeframe, that new potential value of concern is reported in the 40mg column. If the same potential value of concern reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

Programming Notes:

Concomitant Medications

Table 14.3.8.2
Concomitant Medications by ATC Class and Preferred Name
Safety Population

Anatomical Therapeutic Chemical Class (ATC) Preferred Name	40 mg ATH-1017 (N=xxx) n(%)	70 mg ATH-1017 (N=xxx) n(%)	Overall (N=xxx) n(%)
Participants with at least 1 ATC class concomitant medication	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred name 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred name 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)

- ATC: Anatomical Therapeutic Chemical Class; WHO: World Health Organization. N: number of participants in the specified population for given treatment group. Percentages are based on N. A participant with multiple occurrences within an ATC class is counted only once. Concomitant medications (C) are defined as those medications used following the first administration of study drug. Medications started prior to the administration of study drug and continuing into the treatment period are considered as both prior and concomitant medications. WHO Drug Dictionary Version xx used for reporting of medications. Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received. Participants with a C in 70mg will be counted in the 70mg column. If that same participant switched to 40mg and reported a C during the 40mg timeframe, that new C is reported in the 40mg column. If the same C is reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Overall is not a summation of the dose groups.

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NOTE:

- Suggested sorting: ATC classes are presented alphabetically; PNs are sorted within ATC class in descending frequency in the Overall column.

Programming Notes:

- ATC2 and Preferred Term will be used for display.

SECTION 16.X – PARTICIPANT DATA LISTINGS

Discontinued participants

Listing 16.2.1
Participant Disposition
Safety Population

Treatment	Participant ID	AChEI Usage/Age/ Sex/ Race	Site	First Dose Date	Last Dose Date (Day)	Date (Day) of Completion or Discontinuation	Completed or Primary Reason Discontinued (Verbatim)
xxxxxxxx	xxxxxxxx	Y/xx/M/xx	xx	YYYY-MM-DD	YYYY-MM-DD (XX)	YYYY-MM-DD (XX)	Completed
xxxxxxxx	xxxxxxxx	N/xx/F/xx	xx	YYYY-MM-DD	YYYY-MM-DD (XX)	YYYY-MM-DD (XX)	Adverse event (Nausea)
xxxxxxxx	xxxxxxxx	N/xx/F/xx	xx	YYYY-MM-DD	YYYY-MM-DD (XX)	YYYY-MM-DD (XX)	Death
xxxxxxxx	xxxxxxxx	N/xx/F/xx	xx	YYYY-MM-DD	YYYY-MM-DD (XX)	YYYY-MM-DD (XX)	Other (xxxxxxxxxxxxxxxxxxx)

- AChEI: Acetylcholinesterase inhibitor; M: Male; F: Female; Y: Yes; N: No;
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- Day is relative to the first dose date
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

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Programming Notes:

- Please add time also if available.
- Treatment sorting order 40 mg ATH-1017, 70 mg ATH-1017

Listing 16.2.1.1
Participants Reduced to 40mg Dose
Safety Population

Participant ID	AChEI Usage/Age/ Sex/ Race	Parent Study Treatment	Date of First Dose	Date of Dose Reduction (Day)	Reason for Dose Reduction
XXXXXXX	Y/xx/M/xx	ATH1017 xx mg/Placebo	YYYY-MM-DD	YYYY-MM-DD (XX)	xxxxxxxxxx
XXXXXXX	N/xx/F/xx	ATH1017 xx mg/Placebo	YYYY-MM-DD	YYYY-MM-DD (XX)	xxxxxxxxxx
XXXXXXX	N/xx/F/xx	ATH1017 xx mg/Placebo	YYYY-MM-DD	YYYY-MM-DD (XX)	xxxxxxxxxx
XXXXXXX	N/xx/F/xx	ATH1017 xx mg/Placebo	YYYY-MM-DD	YYYY-MM-DD (XX)	xxxxxxxxxx

- Day is relative to first dose date.
- M: Male; F: Female; Y: Yes; N: No; AChEI: Acetylcholinesterase inhibitor
- *Source of dose reduction data to be added as footnote*
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Programming Notes:

- Only include participants with ADSL.DOSE40MG='Y'
- Please add time also if available.

Protocol deviations

Listing 16.2.2
Major Protocol Deviations
Safety Population

Treatment	Participant ID	AChEI Usage/Age/ Sex/ Race	Date of Deviation (Day)	Deviation Category	Descriptions
xxxxxxxx	xxxxxxxx	Y/45/M/xxxx	YYYY-MM-DD (XX)	xxxxxxxxxxx	XXXXXXXXXXXXXXXXXXXXXXXX
			YYYY-MM-DD (XX)	xxxxxxxxxxx	XXXXXXXXXXXXXXXXXXXXXXXX
			YYYY-MM-DD (XX)	xxxxxxxxxxx	XXXXXXXXXXXXXXXXXXXXXXXX
xxxxxxxx	xxxxxxxx	N/49/F/xxxx	YYYY-MM-DD (XX)	xxxxxxxxxxx	XXXXXXXXXXXXXXXXXXXXXXXX

- AChEI: Acetylcholinesterase inhibitor; M: Male; F: Female; Y: Yes; N: No;
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- Day is relative to the first dose date.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Generated from program.sas on DDMMMYYYY HH:MM:SS. Source dataset(s): ADxx. Date of data extraction: DDMMMYYYY. Page X of Y

Programming Notes:

- Please add time also if available.
- Only Major deviations will be displayed.
- Treatment sorting order 40 mg ATH-1017, 70 mg ATH-1017

Demographics and Baseline Characteristics

Listing 16.2.4.1
Participant Demographics and Baseline Characteristics
Safety Population

Treatment	Participant ID	AChEI Usage/Age/ Sex/Race	Ethnicity	Weight (kg)	Height (cm)	BMI (kg/m2)	Years of Education
xxxxxxxx	xxxxxxxx	Y/xx/M/xx	Not Hispanic or Latino	xx	xx	xx	xx
xxxxxxxx	xxxxxxxx	N/xx/F/xx	Not Hispanic or Latino	xx	xx	xx	xx

- BMI: Body Mass Index; AChEI: Acetylcholinesterase inhibitor; M: Male; F: Female; Y: Yes; N: No;
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- Baseline is defined as the last measurement prior to first dose for safety endpoints, and either the measurement on Day 1, or else the last measurement before Day 1 if there is no Day 1 measurement for efficacy endpoints.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Generated from program.sas on DDMMMYYYY HH:MM:SS. Source dataset(s): ADxx. Date of data extraction: DDMMMYYYY. Page X of Y

Programming Notes:

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Listing 16.2.6
Prior and Concomitant Medications
Safety Population

Treatment	Participant ID	P/C	ATC Level 3/ Preferred name/ Reported name	Start Date/Time (Day)/ End Date/Time (Day) / Ongoing	Indication	Dose and units	Frequency	Route
xxxxxxxx	xxxxxxxx	X	xxxxxx/ xxxxxxxxxxx/ xxxxxxxxxxxxx	YYYY-MM-DD HH:MM (XX)/ YYYY-MM-DD HH:MM (XX)	HYPERTENSION	xxx mg	QD	ORAL
xxxxxxxx	xxxxxxxx	X	xxxxxx/ xxxxxxxxxxx/ xxxxxxxxxxxxx	YYYY-MM-DD HH:MM (XX)/ YYYY-MM-DD HH:MM (XX)	DIABETES	xxx mg	QD	ORAL

- P: Prior Medication; C: Concomitant Medication; ATC: Anatomical Therapeutic Chemical.
- Day is relative to the first dose date.
- Prior medications (P) are defined as those medications used prior to the administration of study drug.
- Concomitant medications (C) are defined as those medications used following the first administration of study drug. Medications started prior to the administration of study drug and continuing into the treatment period are considered as both prior and concomitant medications.
- WHO Drug Version xx.x was used for reporting of prior and concomitant medications.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.
- '/' for End Date (Day) means no date was provided.

Generated from program.sas on DDMMMYYYY HH:MM:SS. Source dataset(s): ADxx. Date of data extraction: DDMMMYYYY. Page X of Y

Programming Notes:

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LAB/ECG/VS LISTINGS

Listing 16.2.8.1
Chemistry Laboratory Values Where at Least One Value is a Potential Value of Concern
Safety Population

Treatment	Participant ID	AChEI Usage/ Age/Sex/ Race	Study Visit	Collection Date/Time (Day)	Alkaline Phosphatase (U/L) Observed Value	Alkaline Phosphatase (U/L) Change from Baseline	Alanine Aminotransferase (U/L) Observed Value	Alanine Aminotransferase (U/L) Change from Baseline	Aspartate Aminotransferase (U/L) Observed Value	Aspartate Aminotransferase (U/L) Change from Baseline	Bilirubin (umol/L) Observed Value	Bilirubin (umol/L) Change from Baseline
XXX	xxxxxxx	Y/xx/M/xx	xxxx	YYYY-MM-DDTHH:MM (XX)	xx.xx*	xx.xx	xx.x*	xx.x	xx.xxx*	xx.xxx	xx.xxx*	xx.xxx
			xxxx	YYYY-MM-DDTHH:MM (XX)	xx.xx	xx.xx	xx.x	xx.x	xx.xxx	xx.xxx	xx.xxx	xx.xxx
		N/xx/F/xx	xxxx	YYYY-MM-DDTHH:MM (XX)	xx.xx	xx.xx	xx.x	xx.x	xx.xxx	xx.xxx	xx.xxx	xx.xxx

- AChEI: Acetylcholinesterase inhibitor; Y: Yes; N: No; M: Male; F: Female;
- Race Codes: 1: American Indian or Alaska Native; 2: Asian; 3: Black or African American; 4: Native Hawaiian or Other Pacific Islander; 5: White; 6: Other.
- *Indicates Baseline.
- Baseline is defined as the last measurement prior to first dose.
- Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Generated from program.sas on DDMMMYYYY HH:MM:SS. Source dataset(s): ADxx. Date of data extraction: DDMMMYYYY. Page X of Y

Programming Notes:

- Use code for race.
- Where at least one value for that patient is marked as high or low. Display baseline only if there are High or Low values.
- Run for all Chemistry variables (Albumin (g/L), Alkaline Phosphatase (U/L), Aspartate Aminotransferase (U/L), Bilirubin (umol/L), Calcium (mmol/L), Chloride (mmol/L), Cholesterol (mmol/L), Creatine Kinase (U/L), Creatinine (umol/L), Gamma Glutamyl Transferase (U/L), Glucose (mmol/L), HDL Cholesterol (mmol/L), Hemoglobin A1C (%), LDL Cholesterol (mmol/L), Potassium (mmol/L), Protein (g/L), Protein (g/L), Sodium (mmol/L), Triglycerides (mmol/L).

Listing 16.2.8.2
Hematology Laboratory Values Where at Least One Value is a Potential Value of Concern
Safety Population

- Repeat Listing 16.2.8.1 where at least one value for that patient is marked as high or low.
- Run for all Hematology variables (Basophils (10^9/L), Basophils/Leukocytes (fraction of 1), Eosinophils (10^9/L), Eosinophils/Leukocytes (fraction of 1), Erythrocytes (10^12/L), Hematocrit (fraction of 1), Hemoglobin (g/L), Leukocytes (10^9/L), Lymphocytes (10^9/L), Lymphocytes/Leukocytes (fraction of 1), Monocytes (10^9/L), Monocytes/Leukocytes (fraction of 1), Neutrophils (10^9/L), Neutrophils/Leukocytes (fraction of 1), Platelets (10^9/L)).

Listing 16.2.8.3
Vital Signs Values Where at Least One Value is a Potential Value of Concern
Safety Population

- Repeat Listing 16.2.8.1 where at least one value for that patient is marked as high or low. To identify potential value of concerns, please use the criteria shown below:

Orthostatic Diastolic BP (mmHg)
  Standing Diastolic BP Decrease >=10mmHg
  Standing Diastolic BP Increase >=20mmHg
  Standing Diastolic BP >100mmHg
  Standing Diastolic BP >100 and Increase >=20mmHg
  Standing Diastolic BP <50 and Decrease >=10mmHg
  Standing Diastolic BP <50mmHg

Orthostatic Systolic BP (mmHg)
  Standing Systolic BP Decrease >=20mmHg
  Standing Systolic BP Increase >=20mmHg
  Standing Systolic BP >160mmHg
  Standing Systolic BP >160 and Increase >=20mmHg

Systolic Blood Pressure (mmHg)
  Systolic BP Decrease >=20mmHg
  Systolic BP Increase >=20mmHg
  Systolic BP >160mmHg
  Systolic BP >160 and Increase >=20mmHg

Diastolic Blood Pressure (mmHg)
  Diastolic BP Decrease >=10mmHg
  Diastolic BP Increase >=20mmHg
  Diastolic BP >100 and Increase >=20mmHg
  Diastolic BP <50 and Decrease >=10mmHg

```
  Diastolic BP >100mmHg
  Diastolic BP <50mmHg

Pulse Rate (beats/min)
  Abnormal Heart Rate (<50 or >100 BPM)
  Heart Rate Change >= 30 BPM
```

Listing 16.2.9
ECG Parameters Where at Least One Value is a Potential Value of Concern
Safety Population

Treatment	Participant ID	AChEI Usage/ Age/Sex/ Race	Study Visit	Collection Date/Time (Day)	Parameter (unit)	Abnormality
XXX	xxxxxxx	Y/xx/M/xx	xxxx	YYYY-MM-DDTHH:MM (XX)*	xx (xx)	xxxxxxxxx
					xx (xx)	xxxxxxxxx
					xx (xx)	
					xx (xx)	
					xx (xx)	
					xx (xx)	
					xx (xx)	xxxxxxxxx
					xx (xx)	xxxxxxxxx
			xxxx	YYYY-MM-DDTHH:MM (XX)	xx (xx)	xxxxxxxxx
					xx (xx)	xxxxxxxxx
					xx (xx)	xxxxxxxxx
					xx (xx)	
					xx (xx)	
					xx (xx)	xxxxxxxxx
					xx (xx)	xxxxxxxxx
					xx (xx)	
					xx (xx)	xxxxxxxxx

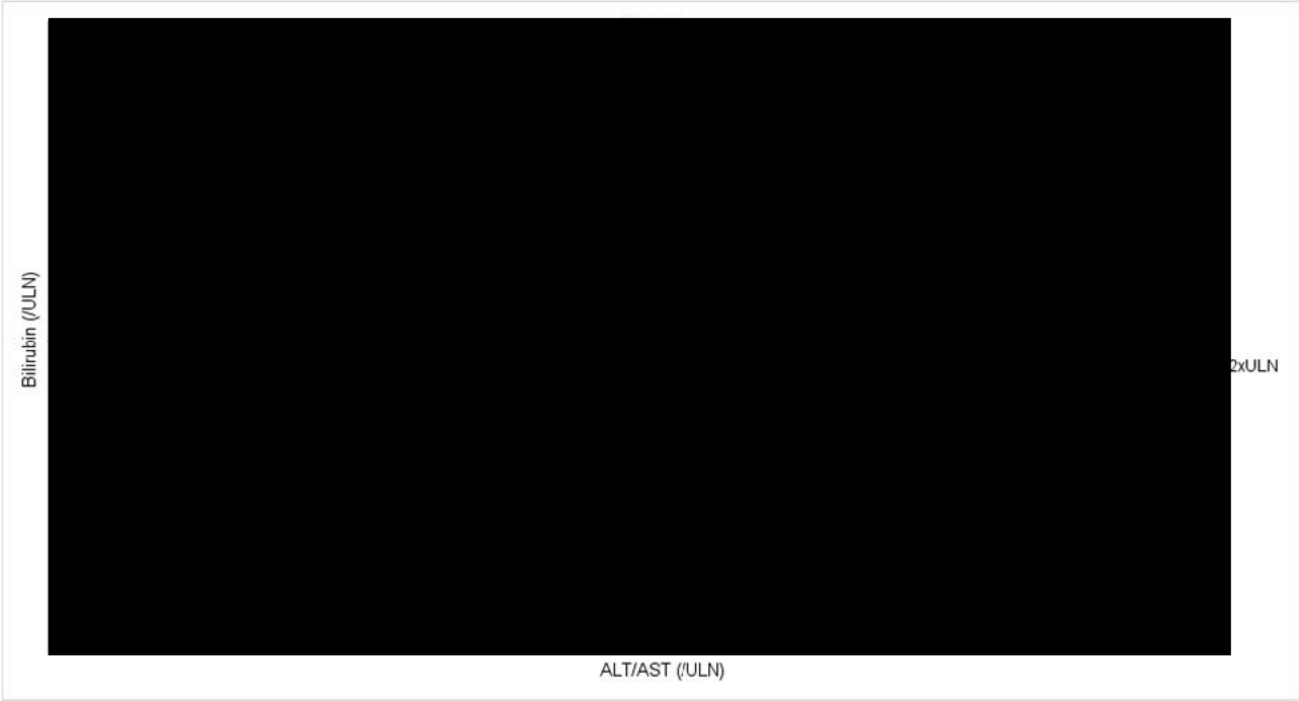
- ECG: Electrocardiogram.
- *Indicates Baseline.
- Baseline is defined as the last measurement prior to first dose.

Programming Notes:

- If at least one parameter has an abnormality for that visit, print all non-missing parameters for that visit, filling in the abnormality column when applicable. Display baseline only if there are abnormal findings.

STANDARD FIGURE SHELLS

Figure 14.3-1.1
eDISH (evaluation of Drug Induced Serious Hepatotoxicity)
Safety Population



- ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; ULN = upper limit of normal. All values were normalized to the ULN that was provided for each participant, lab parameter, and visit. Data displayed in this figure represents the original result as a proportion of ULN.
- Values are the maximum post-baseline. ALT/AST is the maximum Upper Limit of Normal of either ALT or AST.
- Participants with a value in 70mg will be counted in the 70mg group. If that same participant switched to 40mg and reported a value during the 40mg timeframe, that new value is reported in the 40mg group. If the same value is reported while taking 40mg and 70mg then it is counted in both 40mg and 70mg groups; Safety population includes all participants who received at least one dose of study medication, classified by actual treatment received.

Programming Notes:

- 40mg Ath-1017 and 70mg Ath-1017 (no Placebo due to Placebo not in study).