Errata to the FDA Briefing Document
Arthritis Advisory Committee Meeting
August 2, 2017

1. For Table 5, regarding study CNTONAP1001, the fifth column (N per Arm) for sirukumab 100 mg currently reads:

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And should be revised to (change bolded and underlined):

<u>17</u>

2. On page 38, first paragraph under section ARA3003, the second and third sentences currently read:

Approximately 90% of patients completed the 24-week placebo-controlled period on randomized or escape therapy (Table 10). The proportion of patients who discontinued prior to Week 24 was fairly balanced between groups (14% placebo; 19% sirukumab 50 mg q4w, and 16% sirukumab 100 mg q2w)

Should be revised to read (change bolded and underlined):

Approximately **<u>83</u>**% of patients completed the 24-week placebo-controlled period on randomized or escape therapy (Table 10). The proportion of patients who discontinued prior to Week 24 was fairly balanced between groups (14% placebo; 19% sirukumab 50 mg q4w, and **<u>17</u>**% sirukumab 100 mg q2w)

3. On page 52, last paragraph, the current text:

The initial focus of the Agency's safety review was the placebo-controlled phase 3 studies (ARA2002 and ARA2003)

Should be revised to read (change bolded and underlined):

The initial focus of the Agency's safety review was the placebo-controlled phase 3 studies (ARA**<u>3</u>**002 and ARA**<u>3</u>**003)

4. On page 59, Table 29, the correct table footnote should read (change bolded and underlined):

Table 29: Overview of Deaths for Different Safety Pools and Follow-up Times

	ARA3002 and ARA3003			ARA3002 and ARA3003[1]					ARA3002 and ARA3003[1]	
	Through 18 weeks of exposure			Through 52 weeks of exposure					Through SCS cutoff	
	PBO N=850	SIR 50 mg[2] N=848	SIR 100 mg[3] N=850	PBO N=850	SIR 50 mg[2] N=848	SIR 100 mg[3] N=850	SIR Combined[4] 50 mg N=1214	SIR Combined[5] 100 mg N=1217	SIR Combined[4] 50 mg N=1214	SIR Combined[5] 100 mg N=1217
Total patient-years of exposure[6]	292	292	294	520	787	784	1109	1111	1964	1975
Death, N (%[7]), IR	1 (0.1), 0.3	1 (0.1), 0.3	1 (0.1), 0.3	1, 0.2	4, 0.5	6, 0.8	10, 0.9	12, 1.1	15, 0.8	13, 0.7

1 Includes data from ARA3004
2 Only includes patients randomized to sirukumab 50 mg q4w and does not include data after escape/CO in patients initially randomized to placebo who EE/LE/CO to sirukumab 50 mg q4w
3 Only includes patients randomized to sirukumab 100 mg q2w and does not include data after escape/CO in patients initially randomized to placebo who EE/LE/CO to sirukumab 100 mg q2w.
4 All patients who received at least one dose of sirukumab 50 mg q4w through the noted exposure time. This includes patients who were initially randomized to sirukumab 50mg q4w and patients randomized to placebo who EE/LE/CO to sirukumab 50 mg q4w.
5 All patients who received at least one dose of sirukumab 100 mg q2w through the noted exposure time. This includes patients who were initially randomized to sirukumab 100 mg q2w and patients randomized to placebo who EE/LE/CO to sirukumab 100 mg q2w.
6 Total patient-years of exposure is calculated as the total amount of safety follow-up in the given window with censoring due to lost to follow-up, completion of planned follow-up, or window cutoff
7 Cumulative incidence percentages are only shown through 18 weeks and no other time periods given differences in exposure between sirukumab and placebo after 18 weeks.
Abbreviations: PBO=placebo; SIR=sirukumab; EE=early escape; LE=late escape; CO=cross over; SCS=Summary of Clinical Safety; IR=incidence rate per 100 person years; q2w=every 2 weeks; q4w=every 4 weeks
Sirukumab doses: sirukumab 50 mg every 4 weeks and sirukumab 100 mg every 2 weeks
Source: IR response, page 128, submitted 5/26/17

This same footnote change applies to Table 35 (page 65), Table 37 (page 67), Table 47 (page 79), Table 48 (page 81), Table 51 (page 83), Table 54 (page 86), and Table 55 (page 87).

5. On page 62, Table 32, the correct table should read (change with strikethrough or bolded and underlined):

Table 32: Incidence Rate (Subject Based Per 100 Patient-Years of Follow-up) of Death Overall and by Cause in the Sirukumab RA Development Program (All Subject Analysis Set)

	Sirukumab (n=3,120)	
~~Study~~	Number of deaths	Incidence per 100 PY, 95% CI
All cause of death (as assessed by the investigator)	34[a,b]	0.75 (0.52, 1.04)
MACE	13	0.29 (0.15, 0.49)
Malignancy	6	0.13 (0.05, 0.29)
Serious infection	8	0.18 (0.08, 0.35)
Other causes	9	0.20 (0.09, 0.38)

a The deaths listed in this table are only for patients exposed to sirukumab and this table does not include the one death on placebo
b Patients could have more than one cause of death as attributed by the investigator
Abbreviations: MACE=major adverse cardiovascular event; RA=rheumatoid arthritis; PY=patient years; CI=confidence interval
Source: Summary of Clinical Safety—Correction Report, Table 15, page 9, received 6/12/17

6. On page 73, Table 42, a footnote from the Applicant's information request response was not included and has been added below (change bolded and underlined):

Table 42: AST, ALT, and Bilirubin Laboratory Changes by Multiples of the Upper Limit of Normal through 18 Weeks of Exposure (ARA3002 and ARA3003)

	ARA3002 and ARA3003 Through 18 weeks of exposure		
	PBO N=850	SIR 50 mg N=848	SIR 100 mg N=850
Patients with any event of ALT >ULN, %	21.2	58.3	57.1
Patients with any event of ALT≥3x ULN, %	1.3	6.3	8.2
Patients with any event of ALT≥5x ULN, %	0.6	1.7	2.1
Patients with any event of ALT≥8xULN, %	0.2	0.5	0.8
Patients with any event of AST >ULN, %	16.2	44.6	44.7
Patients with any event of AST≥3x ULN, %	0.7	2.4	3.4
Patients with any event of AST≥5x ULN, %	0.4	0.2	0.7
Patients with any event of AST≥8xULN, %	0.2	0	0.1
Patients with any event of total bilirubin >ULN, %	1.2	9.4	11.8

Data presented utilizes the last scheduled visit on/prior to the end of the analysis period and the mean change for that visit. For patients who discontinued prior to the last scheduled visit on or prior to the end of the analysis period were not included.
Abbreviations: PBO=placebo; SIR=sirukumab; EE=early escape; LE=late escape; CO=cross over; q2w=every 2 weeks; q4w=every 4 weeks
Sirukumab doses: sirukumab 50 mg every 4 weeks and sirukumab 100 mg every 2 weeks
Source: IR Response, page 132, submitted 5/26/17

7. On page 99, paragraph 1, line 7, the sentence should read:

The model included the following as covariates: visit week, treatment, and treatment-by-week interaction.

Should be revised to read (change with strikethrough):

The model included the following as covariates: visit week, ~~treatment,~~ and treatment-by-week interaction.