PFIZER INC.

These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert.

COMPOUND NUMBER: ATN-103

PROTOCOL NO.: 3242K1-2003-WW (B2271005)

PROTOCOL TITLE:

An Open-Label, Extension Study to Assess the Long Term Safety and Tolerability of ATN-103 in Subjects With Rheumatoid Arthritis

Study Centers:

A total of 103 centers in 10 countries took part in the study and a total of 67 centers in 8 countries enrolled subjects; 26 centers in the United States (US), 19 in Japan, 8 in Russian Federation, 4 each in Canada and South Africa, 3 in Hungary, 2 in Serbia and 1 in Switzerland.

Study Initiation Date and Final Completion Date:

15 February 2010 and 08 February 2012

Phase of Development:

Phase 2

Study Objective:

To evaluate the long-term safety and tolerability of ATN-103 administered subcutaneously (SC) to subjects with rheumatoid arthritis (RA).

METHODS:

Study Design:

This was a multicenter, open-label extension study to evaluate the long-term safety and tolerability of ATN-103 administered SC every 4 weeks (Q4W) to subjects with RA. The study consisted of a 48 week open-label treatment period and an 8 week Post-Treatment Follow-Up period, thus the anticipated duration of subject's participation in the study was 56 weeks. Eligible subjects had completed 1 of 2 previous double-blind, placebo-controlled studies (3242K1-2000-WW: A Seamless, Phase 1/2, Multiple Ascending Dose, Proof of Concept Study of ATN-103 Administered to Subjects With Active Rheumatoid Arthritis on a Background of Methotrexate [NCT00959036] or 3242K1-2001-JA: A Randomized, Multicenter, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study of the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Clinical Efficacy of ATN-103 Administered to Japanese Subjects With Active Rheumatoid Arthritis on a Background of Methotrexate [NCT01007175]), signed an informed consent form (ICF) for the current study 3242K1-2003-WW, and met the entry criteria at the Baseline Visit. The Week 20 Visit

(Follow-Up Visit) in studies 3242K1-2000-WW and 3242K1-2001-JA corresponded to the Baseline Visit in this study.

The 3242K1-2000-WW double-blind study was a seamless adaptive multiple ascending dose (MAD) / proof-of-concept (POC) study that assessed the safety and efficacy of 5 dose-level/frequency combinations of ATN-103 (10 mg, 30 mg, or 80 mg administered SC Q4W and 10 mg or 80 mg administered SC every 8 weeks [Q8W]). As the 3242K1-2000-WW study progressed, a data monitoring committee performed unblinded safety and efficacy reviews of the various doses being studied relative to placebo. Based on the results of this study, the ATN-103 dose and regimen were carried forward in the open-label extension study (3242K1-2001-JA).

The 3242K1-2001-JA study was a MAD study that included dose/frequency combinations identical to those utilized in study 3242K1-2000-WW. The focus of study 3242K1-2001-JA was the safety and tolerability of ATN-103 in Japanese subjects with RA. ATN-103 was safe and generally well tolerated at SC doses of 10 mg, 30 mg, and 80 mg administered Q4W schedule and at doses of 10 mg and 80 mg administered Q8W schedule.

In this open-label extension study all subjects received ATN-103 given an SC injection on a Q4W schedule. Initially, all subjects received an ATN-103 starting dose of 10 mg. Subsequently, during the first 12 weeks of this study, the monthly ATN-103 dose that a subject received could be increased by the Investigator based on that subject's individual response to treatment as assessed by the Clinical Disease Activity Index (CDAI) and an assessment of subject safety. Subjects with a high RA disease activity (CDAI >22) at the Week 4 or 8 Visit had their ATN-103 dose increased to the next higher available ATN-103 dose-level at that Visit. Subjects with moderate to high RA disease activity (CDAI >10) at Week 12 had their ATN-103 dose increased to the next higher available ATN-103 dose-level at that Visit. The Investigator decreased a dose if the subject did not tolerate the dose-level. No dose adjustments based on individual subject response were allowed after the Week 12 Visit.

During the conduct of this study, the final results of the 3242K1-2000-WW Phase 2, POC study became available and demonstrated that the 80 mg dose of ATN-103 administered once Q4W showed clinically and statistically significant efficacy (American College of Rheumatology ≥20% improvement criteria [ACR20] response) compared to placebo at Week 16 (primary endpoint). ATN-103 at 30 mg given Q4W showed some improvement in ACR20 response at Week 16 but it was not statistically significant compared to placebo. The results with ATN-103 10 mg once Q4W were similar to placebo. There were no dose related increases in adverse events (AEs) or serious adverse events (SAEs). Based on these results, the protocol was amended so that the 10 mg dose was discontinued in this open-label extension study. Irrespective of study week, all subjects who were still in the treatment phase of the study when this protocol amendment was implemented at their site and who were receiving 10 mg Q4W increased their dose to 30 mg or 80 mg once Q4W. All subjects receiving 30 mg Q4W and had a CDAI score >22 increased their dose to 80 mg once Q4W. Similarly, all subjects who were receiving 30 mg once Q4W and had a CDAI score ≤22, were to be considered for dose increase to 80 mg once Q4W because of the possibility of an increased clinical response. The decision to increase the dose was based upon the

Investigator's assessment of the subject's response to treatment following discussion of the results of study 3242K1-2000-WW with the subject.

Subjects could have withdrawn from the study at any time because of a therapeutic response that was deemed clinically inadequate. If, from Visit 6 (Week 20) to Visit 13 (Week 48 End of Treatment Period), the CDAI score of a subject receiving 80 mg ATN-103 Q4W was >22 at any 2 consecutive Visits, the physician determined in conjunction with the subject whether or not it was in the subject's best interest to continue in the study or to withdraw and pursue alternative therapy. If the decision was made to withdraw the subject from the study, the subject was asked to complete the early withdrawal procedures and documentation of the reason for early withdrawal was to be included in the subject's file. At the completion of the open-label treatment period, the subjects entered an 8 week follow-up period.

Number of Subjects (Planned and Analyzed):

It was estimated that approximately 260 subjects would participate in this extension study. Subjects who had completed the Week 20 Follow-Up Visit in the preceding double-blind studies 3242K1-2000-WW and 3242K1-2001-JA and qualified for this study per the inclusion/exclusion criteria, and wished to participate, were enrolled. A total of 267 subjects were screened in 67 centers and 8 countries, 266 subjects were enrolled, started open-label treatment, received at least 1 dose of study medication and thus were included in the safety population.

Of the 266 subjects, 92 subjects were enrolled in the US, 55 in Japan, 45 in Russian, Federation, 38 in South Africa, 11 each in Canada and Hungary, 8 in Serbia and 6 in Switzerland.

Diagnosis and Main Criteria for Inclusion and Exclusion:

Subjects who had completed study 3242K1-2000-WW or 3242K1-2001-JA and had no events that, in the opinion of the Investigator, would have precluded entry or participation in this study.

Main Exclusion Criteria: Pregnant or nursing women of subjects with any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, cardiovascular, hematological, gastrointestinal, endocrine, pulmonary, immunologic [eg, Felty syndrome, human immunodeficiency virus infection], infectious, neurological, or cerebral psychiatric disease, or evidence of demyelinating disease) that, in the Investigator's judgment, would substantially increase the risk associated with the subject's developing an AE or SAE during the study, or preclude the evaluation of the subject's response, were excluded from the study.

Study Treatment:

Investigational product was provided as 160 mg ATN-103 in 5 mL flint glass vials, to be reconstituted with 1.3 mL of sterile water (provided in 10 mL flint glass vials) for a final volume of 1.6 mL for SC injection. After reconstitution, each vial provided an extractable volume of 1.0 mL of ATN-103 at a concentration of 100 mg/mL. All study medication was packaged and labeled according to regulatory requirements and supplied at study centers by

the Sponsor. A sterile polypropylene, latex-free 1.0 mL syringe was used for drug administration.

Each subject received a single SC injection of ATN-103 Q4W. There were approximately 13 SC injections during the study. Each subject was given a single SC injection of ATN-103 at every scheduled Visit during the treatment period.

Safety Endpoints:

Physical examinations, vital sign measurements, laboratory evaluations, recording of early withdrawal, recording of AEs and SAEs, immunogenicity assessment, assessment of injection site reactions (ISRs).

Efficacy, pharmacokinetic and pharmacodynamic endpoints were considered exploratory and are not reported here. No further analysis of pharmacokinetic data was conducted due to discontinuation of ATN-103 development by the Sponsor.

Safety Evaluations:

Safety assessments included vital signs (weight, blood pressure, pulse rate, respiratory rate, and temperature were conducted at Screening/Baseline, every 4 weeks thereafter and at the time of early withdrawal), routine laboratory measurements (clinical laboratory evaluations were conducted at Screening/Baseline, Weeks 12, 24, 36, 48 or at the time of early withdrawal), physical examination, AEs and SAEs (including medically important infections, ISRs, and cancers) from the time the ICF had been signed (at Baseline) to the Follow-up Visit, and proportions of subjects with predefined clinically important (PCI) events, premature discontinuations and non-study medications, and immunogenicity assessment (blood samples were collected prior to SC administration of investigational product to determine concentrations of anti-ATN-103 antibodies and neutralizing antibodies at Baseline [from the last Visit of preceding studies], Weeks 12, 24, 36, and 48 or early withdrawal).

Statistical Methods:

All subjects who received at least 1 dose of investigational product in this extension study were included in the safety (safety population) analyses.

RESULTS:

Subject Disposition and Demography:

Subject disposition is summarized in Table 1. Of the 267 subjects screened, 266 (99.6%) subjects were enrolled, started open-label treatment, received at least 1 dose of study medication, and thus were included in the safety population. Overall, 37 (13.9%) subjects withdrew from the study, and the most common reasons for subject discontinuation were AEs in 14 (5.3%) subjects and unsatisfactory response-efficacy in 13 (4.9%) subjects.

Table 1. Summary of Subject Disposition

Population Group	Number (%) of Subjects
Screened	267 (100.0)
Screen failures	1 (0.4)
Randomized	266 (99.6)
Enrolled but not treated	0
Study completed	229 (86.1)
Discontinued	37 (13.9)
Adverse event	14 (5.3)
Failed to return	3 (1.1)
Investigator request	2 (0.8)
Other	1 (0.4)
Subject request	4 (1.5)
Unsatisfactory response-efficacy	13 (4.9)
Safety population	266 (99.6)

Of the 266 subjects, 53 (19.92%) were men and 213 (80.08%) were women, with an age range of 18 to 79 years, and a median age of 53 years. A summary of demographic and baseline characteristics is presented in Table 2.

Table 2. Demographic Characteristics and Baseline Characteristics - Safety Population

Characteristic	ATN-103
Number of Subjects	**266**
Age (years):	
Mean	52.11
SD	12.08
Range	18.00-79.00
Median	53.00
Sex, n (%):	
Male	53 (19.92)
Female	213 (80.08)

n = number of subjects with specified criteria; SD = standard deviation.

Safety Results:

Serious Adverse Events: Overall 55 SAEs were reported by 35 (13.2%) subjects, including 2 subjects who each experienced post-study SAEs (ie, an SAE with onset >30 days post last dose of study medication), and a summary of these SAEs is presented in Table 3.

Table 3. Treatment-Emergent Serious Adverse Events (All-Causality)

System Organ Class[a] Preferred Term	ATN-103 N=266 n (%)
Subjects with any serious adverse event[b]	35[b] (13.2)
Blood and lymphatic system disorders	1 (0.4)
Hypochromic anaemia	1 (0.4)
Cardiac disorders	7 (2.6)
Angina pectoris	1 (0.4)
Atrial fibrillation	3 (1.1)
Myocardial infarction	3 (1.1)
Congenital, familial and genetic disorders	1 (0.4)
Trisomy 21	1 (0.4)
Ear and labyrinth disorders	1 (0.4)
Vertigo	1 (0.4)
Gastrointestinal disorders	4 (1.5)
Duodenal ulcer perforation	1 (0.4)
Inguinal hernia	1 (0.4)
Pancreatitis	2 (0.8)
General disorders and administration site conditions	1 (0.4)
Device dislocation	1 (0.4)
Hepatobiliary disorders	1 (0.4)
Cholecystitis acute	1 (0.4)
Immune system disorders	1 (0.4)
Hypersensitivity	1 (0.4)
Infections and infestations	6 (2.3)
Bronchitis	1 (0.4)
Pneumonia	1 (0.4)
Pneumonia legionella	1 (0.4)
Sepsis	1 (0.4)
Tuberculosis of intrathoracic lymph nodes	1 (0.4)
Viral infection	1 (0.4)
Wound infection bacterial	1 (0.4)
Wound infection pseudomonas	1 (0.4)
Injury, poisoning and procedural complications	6 (2.3)
Femur fracture	1 (0.4)
Fibula fracture	1 (0.4)
Lower limb fracture	1 (0.4)
Post procedural haemorrhage	1 (0.4)
Radius fracture	1 (0.4)
Synovial rupture	1 (0.4)
Tibia fracture	1 (0.4)
Investigations	1 (0.4)
Haemoglobin decreased	1 (0.4)
Metabolism and nutrition disorders	1 (0.4)
Hyperkalaemia	1 (0.4)
Musculoskeletal and connective tissue disorders	4 (1.5)
Intervertebral disc protrusion	1 (0.4)
Osteoarthritis	1 (0.4)
Rheumatoid arthritis	1 (0.4)
Spinal osteoarthritis	1 (0.4)

Table 3. Treatment-Emergent Serious Adverse Events (All-Causality)

System Organ Class[a] Preferred Term	ATN-103 N=266 n (%)
Subjects with any serious adverse event[b]	35[b] (13.2)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	4 (1.5)
Colon cancer	1 (0.4)
Lung adenocarcinoma	1 (0.4)
Meningioma benign	1 (0.4)
Prostate cancer	1 (0.4)
Nervous system disorders	1 (0.4)
Vascular encephalopathy	1 (0.4)
Pregnancy, puerperium and perinatal conditions	1 (0.4)
Abortion spontaneous	1 (0.4)
Psychiatric disorders	2 (0.8)
Acute psychosis	1 (0.4)
Depression	1 (0.4)
Disorientation	1 (0.4)
Renal and urinary disorders	1 (0.4)
Renal failure acute	1 (0.4)
Respiratory, thoracic and mediastinal disorders	5 (1.9)
Interstitial lung disease	2 (0.8)
Pulmonary embolism	2 (0.8)
Respiratory failure	1 (0.4)
Vascular disorders	1 (0.4)
Deep vein thrombosis	1 (0.4)
Hypotension	1 (0.4)

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AE = adverse event; N = total number of subjects; n = number of subjects with specified criteria;
SAE = serious adverse event.

a. Totals for the number of subjects at a higher level were not necessarily the sum of those at the lower levels since a subject could have reported ≥2 different AEs within the higher level category.
b. Including 2 subjects that experienced post-study SAEs (ie, SAEs with onset >30 days post last dose of study medication).

Treatment-Emergent Treatment-Related Serious Adverse Events: Five (5) subjects experienced SAEs that were considered related to the investigational product by the Investigator. Table 4 presents treatment-emergent treatment-related SAEs reported during the study.

Table 4. Treatment-Emergent Treatment-Related Serious Adverse Events

ATN-103 10 mg Every 4 weeks			
Serial Number	**System Organ Class[a]**	**Preferred Term[a]**	**Outcome**
1	Cardiac disorders	Myocardial infarction	Resolved
2	Infections and infestations	Pneumonia	Resolved
3	Infections and infestations	Pneumonia legionella	Resolved
4	Neoplasms benign, malignant and unspecified (including cysts and polyps)	Lung adenocarcinoma	Persisted
5	Respiratory, thoracic and mediastinal disorders	Interstitial lung disease	Persisted

a. Medical Dictionary for Regulatory Activities (MedDRA) is applied.

Adverse Events: Table 5 presents treatment-emergent AEs (TEAEs) - all-causalities reported in ≥2% of population.

Table 5. Treatment-Emergent Adverse Events (All-Causality) Reported in ≥2% of Safety Population

System Organ Class[a] Preferred Term[a]	Treatment ATN-103 N=266 n (%)
Any adverse event	169 (63.5)
Blood and lymphatic system disorders	9 (3.4)
Ear and labyrinth disorders	6 (2.3)
Eye disorders	14 (5.3)
Gastrointestinal disorders	42 (15.8)
General disorders and administration site conditions	17 (6.4)
Hepatobiliary disorders	7 (2.6)
Immune system disorders	6 (2.3)
Infections and infestations	98 (36.8)
Nasopharyngitis	22 (8.3)
Sinusitis	12 (4.5)
Upper respiratory tract infection	23 (8.6)
Urinary tract infection	11 (4.1)
Injury, poisoning and procedural complications	20 (7.5)
Investigations	31 (11.7)
Alanine aminotransferase increased	10 (3.8)
Aspartate aminotransferase increased	8 (3.0)
Metabolism and nutrition disorders	9 (3.4)
Musculoskeletal and connective tissue disorders	26 (9.8)
Back pain	6 (2.3)
Rheumatoid arthritis	6 (2.3)
Nervous system disorders	21 (7.9)
Headache	8 (3.0)
Psychiatric disorders	13 (4.9)
Respiratory, thoracic and mediastinal disorders	16 (6.0)
Skin and subcutaneous tissue disorders	36 (13.5)
Rash	8 (3.0)
Vascular disorders	11 (4.1)
Hypertension	11 (4.1)

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
N = total number of subjects; n = number of subjects with specified criteria.
a. Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report 2 or more different adverse events within the higher level category.

Treatment-Emergent Treatment-Related Adverse Events: Sixty-six (66 [24.8%]) subjects experienced ≥1 TEAE that was considered related to study drug treatment by the Investigator. Table 6 presents the treatment-emergent treatment-related AEs during the study.

Table 6. Treatment-Emergent Treatment-Related Adverse Events Reported During the Study

System Organ Class[a] Preferred Term[a]	Treatment ATN-103 N=266 n (%)
Any treatment-related AE	66 (24.8)
Cardiac disorders	1 (0.4)
Myocardial infarction	1 (0.4)
Ear and labyrinth disorders	1 (0.4)
Vertigo	1 (0.4)
Endocrine disorders	1 (0.4)
Thyroiditis chronic	1 (0.4)
Eye disorders	4 (1.5)
Conjunctivitis	2 (0.8)
Conjunctivitis allergic	1 (0.4)
Dry eye	1 (0.4)
Scleritis	1 (0.4)
Vision blurred	1 (0.4)
Gastrointestinal disorders	13 (4.9)
Abdominal pain	1 (0.4)
Abdominal pain upper	1 (0.4)
Constipation	2 (0.8)
Dental caries	1 (0.4)
Diarrhea	1 (0.4)
Gastric disorder	1 (0.4)
Gastritis erosive	1 (0.4)
Gingival pain	1 (0.4)
Hiatus hernia	1 (0.4)
Lip disorder	1 (0.4)
Nausea	2 (0.8)
Radicular cyst	1 (0.4)
Sensitivity of teeth	1 (0.4)
Stomatitis	2 (0.8)
Vomiting	1 (0.4)
General disorders and administration site conditions	5 (1.9)
Injection site haemorrhage	1 (0.4)
Malaise	2 (0.8)
Edema peripheral	1 (0.4)
Pyrexia	2 (0.8)
Hepatobiliary disorders	3 (1.1)
Hepatic function abnormal	2 (0.8)
Hepatic steatosis	1 (0.4)
Immune system disorders	2 (0.8)
Allergy to arthropod sting	1 (0.4)
Drug hypersensitivity	1 (0.4)
Infections and infestations	40 (15.0)
Bronchitis	1 (0.4)
Clostridial infection	1 (0.4)
Empyema	1 (0.4)
Enterocolitis infectious	1 (0.4)
Escherichia infection	1 (0.4)
Folliculitis	1 (0.4)
Gastroenteritis	2 (0.8)

Table 6. Treatment-Emergent Treatment-Related Adverse Events Reported During the Study

System Organ Class[a] Preferred Term[a]	Treatment ATN-103 N=266 n (%)
Herpes zoster	1 (0.4)
Impetigo	1 (0.4)
Influenza	2 (0.8)
Intertrigo candida	1 (0.4)
Nasopharyngitis	13 (4.9)
Onychomycosis	1 (0.4)
Oral herpes	1 (0.4)
Otitis media	1 (0.4)
Paronychia	1 (0.4)
Pharyngitis	3 (1.1)
Pneumonia	2 (0.8)
Pneumonia legionella	1 (0.4)
Pyelonephritis	1 (0.4)
Rhinitis	1 (0.4)
Sinusitis	2 (0.8)
Tinea faciei	1 (0.4)
Tinea pedis	2 (0.8)
Tonsillitis	2 (0.8)
Upper respiratory tract infection	9 (3.4)
Urinary tract infection	3 (1.1)
Viral infection	1 (0.4)
Investigations	19 (7.1)
Alanine aminotransferase increased	7 (2.6)
Antinuclear antibody increased	4 (1.5)
Antinuclear antibody positive	1 (0.4)
Aspartate aminotransferase increased	5 (1.9)
Cardiolipin antibody positive	3 (1.1)
Chest X-ray abnormal	1 (0.4)
Haemoglobin decreased	1 (0.4)
Liver function test abnormal	2 (0.8)
Tuberculin test positive	1 (0.4)
Urine leukocyte esterase positive	1 (0.4)
White blood cell count decreased	1 (0.4)
White blood cell count increased	1 (0.4)
Metabolism and nutrition disorders	2 (0.8)
Hypercholesterolaemia	2 (0.8)
Musculoskeletal and connective tissue disorders	4 (1.5)
Back pain	1 (0.4)
Lumbar spinal stenosis	1 (0.4)
Muscle spasms	1 (0.4)
Pain in extremity	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.4)
Lung adenocarcinoma	1 (0.4)
Nervous system disorders	5 (1.9)
Dizziness	2 (0.8)
Essential tremor	1 (0.4)
Headache	2 (0.8)
Paraesthesia	1 (0.4)

Table 6. Treatment-Emergent Treatment-Related Adverse Events Reported During the Study

System Organ Class[a] Preferred Term[a]	Treatment ATN-103 N=266 n (%)
Post herpetic neuralgia	1 (0.4)
Psychiatric disorders	4 (1.5)
Insomnia	2 (0.8)
Major depression	1 (0.4)
Sleep disorder	1 (0.4)
Respiratory, thoracic and mediastinal disorders	6 (2.3)
Bronchitis chronic	1 (0.4)
Interstitial lung disease	2 (0.8)
Pulmonary fibrosis	1 (0.4)
Rhinitis allergic	2 (0.8)
Skin and subcutaneous tissue disorders	9 (3.4)
Acne	1 (0.4)
Dermatitis	1 (0.4)
Exfoliative rash	1 (0.4)
Nail disorder	1 (0.4)
Pruritus	1 (0.4)
Psoriasis	1 (0.4)
Rash	1 (0.4)
Rash generalised	1 (0.4)
Scar	1 (0.4)
Urticaria	1 (0.4)
Vascular disorders	2 (0.8)
Hypertension	2 (0.8)

AEs and SAEs are not separated out in this table.
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA).
AE = adverse event; N = Total number of subjects; n = number of subjects with specified criteria;
SAE = serious adverse event.
a. Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report 2 or more different AEs within the higher level category.

Permanent Discontinuations due to Adverse Events: Permanent discontinuations due to AEs were reported for 14 (5.3%) subjects, and 11 of these subjects were withdrawn due to SAEs. The most frequent AE leading to discontinuation from the study was interstitial lung disease (3 subjects).

Death: No deaths were reported during the study.

Auto-Antibodies: A summary of auto-antibodies status and the number of subjects testing positive for auto-antibodies by study time point is presented in Table 7.

Table 7. Summary of Auto-Antibodies Status And Number (%) Subjects Testing Positive - Tested by Study Timepoint - Safety Population

Timepoints	Observations			
	Anti Cardiolipin IgG (n/N [%])	Anti Cardiolipin IgM (n/N [%])	Anti DS DNA (n/N [%])	Antinuclear AB (n/N [%])
Positive at any time	54/ 266 (20.30)	136/266 (51.13)	43/266 (16.17)	205/266 (77.07)
Positive at Baseline	23/ 266 (8.65)	61/266 (22.93)	18/266 (6.77)	120/266 (45.11)
Positive at Last Visit	30/ 266 (11.28)	98/266 (36.84)	25/266 (9.40)	169/266 (63.53)
From negative at Baseline to positive at Last Visit	18/ 243 (7.41)	52/205 (25.37)	20/248 (8.06)	63/146 (43.15)
From positive at Baseline to negative at Last Visit	11/ 23 (47.83)	15/61 (24.59)	13/18 (72.22)	14/120 (11.67)
Baseline	23/266 (8.65)	61/266 (22.93)	18/266 (6.77)	120/266 (45.11)
Week 12	22/253 (8.70)	74/253 (29.25)	14/242 (5.79)	139/257 (54.09)
Week 24	33/238 (13.87)	74/238 (31.09)	16/238 (6.72)	137/241 (56.85)
Week 36	23/226 (10.18)	74/226 (32.74)	19/225 (8.44)	135/226 (59.73)
Week 48	29/229 (12.66)	84/228 (36.84)	22/229 (9.61)	153/230 (66.52)

Baseline values are the last evaluation from the preceding double-blind studies.
AB = antibody; DNA = deoxyribonucleic acid; DS = double stranded; IgG = Immunoglobulin G; IgM = Immunoglobulin M; N = total number of subjects; n = number of subjects with positive value.

Antinuclear Antibodies: Overall, 58 of 123 (47.15%) subjects negative at Baseline were positive for antinuclear antibodies at Week 48, and 12 of 107 (11.21%) subjects positive for antinuclear antibodies at Baseline were negative at Week 48. A total of 85 of 146 subjects (58.22%) negative at Baseline tested positive on at least 1 occasion on treatment, and 7 of 120 subjects (5.83%) positive at Baseline tested negative on all occasions.

Anti-Double-Stranded Deoxyribonucleic Acid: For ATN-103, 17 of 211 subjects (8.06%) negative at Baseline were positive for anti-double-stranded deoxyribonucleic acid (DNA) antibodies at Week 48 and 13 of 18 subjects (72.22%) who converted from negative at Baseline to positive at Week 48 in anti-double-stranded DNA. Twenty-five (25), of 248 subjects (10.08%) negative at Baseline, tested positive on at least 1 occasion on treatment and 10 of 18 (55.56%) subjects positive at Baseline tested negative on all occasions on treatment.

Anti-Cardiolipin Immunoglobulin G: For ATN-103, 16 of 206 subjects (7.77%) negative for anti-cardiolipin Immunoglobulin G at baseline were positive at Week 48, and 10 of 23 subjects (43.48%) positive at Baseline were negative at Week 48. Thirty-one (31) of 243 subjects (12.76 %) negative at Baseline tested positive on at least 1 occasion on treatment, and 5 of 23 subjects (21.74%) positive at Baseline tested negative on all occasions on treatment.

Anti-Cardiolipin Immunoglobulin M: For ATN-103, 46 of 177 subjects (25.99%) negative at Baseline tested positive for anti cardiolipin Immunoglobulin M at Week 48, and 13 of 51 subjects (25.49%) positive at Baseline tested negative at Week 48. A total of 75 of

205 (36.59%) negative at Baseline tested positive on at least 1 occasion on treatment, and 6 of 61 subjects (9.84%) positive at Baseline tested negative on all occasions on treatment.

Injection Site Reactions: One (1) subject experienced swelling in upper right arm on the day of administration of the subject's Week 40 injection at a dose of 80 mg, and 1 subject experienced redness in abdomen (injection site) after receiving baseline, Week 8, Week 12, Week 16, Week 24, Week 28 and Week 32 injections at the 10 mg dose. All the ISRs resolved without any clinical action being taken.

Plasma Immunogenicity: A total of 7/265 (2.64%) subjects were tested positive for neutralizing antibodies at any time during the study.

Efficacy endpoints were considered exploratory and hence the results are not reported here.

CONCLUSION:

In general, treatment with ATN-103 was well tolerated. The AE profile in this long-term extension study was consistent with that seen in the 2 preceding studies.