2.0 Synopsis

AbbVie Inc.	**Individual Study Table Referring to Part of Dossier:** **Volume:** **Page:**	**(For National Authority Use Only)**
Name of Study Drug: Adalimumab		
Name of Active Ingredient: Adalimumab		

Title of Study: A Phase 3, Multicenter, Double-Blind, Randomized, Parallel-Arm, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Adalimumab for Treatment of Nail Psoriasis in Subjects with Chronic Plaque Psoriasis

Investigator: Boni Elewski, MD, [redacted] AL [redacted]

Study Sites: Subjects were enrolled at 32 sites in Australia, Belgium, Canada, France, Germany, Greece, Puerto Rico, and the United States

Publications: None

Studied Period (Years): First Subject First Visit: 30 January 2014 Last Subject Last Visit: 27 April 2016	**Phase of Development:** 3

Objectives:

The primary objective of this study was to evaluate the safety and efficacy of adalimumab for treatment of nail psoriasis. The study was also designed to evaluate the pharmacokinetics and safety of adalimumab in subjects with nail psoriasis.

Methodology:

This is a Phase 3, multicenter, double-blind, randomized, parallel-group, placebo controlled study, designed to demonstrate the safety and efficacy of adalimumab in the treatment of nail psoriasis.

The study consists of a 3- to 35-day screening period, a 26-week double-blind, placebo-controlled treatment period (Period A), a 26-week open-label extension period (Period B), and a 70-day safety follow-up period.

Eligible subjects were randomized 1:1 at Baseline (Week 0) to either 40 mg of adalimumab every other week (eow) starting 1 week after the initial dose of 80 mg or placebo (PBO). The randomization was stratified by center. Subjects who completed Period A were able to participate in an open-label extension period, Period B. Subjects from the PBO treatment group received blinded injections of 80 mg adalimumab and subjects from the adalimumab treatment group received matching PBO at Week 26. All subjects received open-label adalimumab 40 mg eow from Week 27 to Week 51. No medication was dispensed or injected at Week 52.

Methodology (Continued):

The 70-day safety follow-up period started from the last dose of study drug, but was not required for any subject who initiated commercial Humira after study completion.

Additional visits for clinical and safety assessments were performed at Weeks 4, 8, 12, 16, 21, 25, 26, 28, 36, 44, 51, and 52 or premature discontinuation (PD). Blood samples for adalimumab pharmacokinetic (PK), anti-adalimumab antibody (AAA) assays and biomarker analysis were collected. Subjects who consented to participate in the optional pharmacogenetic (PG) analysis had additional samples drawn.

Starting from Week 16, if body surface area (BSA) affected by psoriasis had increased by 25% or more over the Baseline measurement, subjects rolled over to the open-label extension period of the study (Period B).

Subjects were discontinued from the study if they withdrew consent or if they were deemed unsuitable to continue for any reason by the Investigator.

Number of Subjects (Planned and Analyzed):

Planned: Approximately 200 subjects

Analyzed: 217 subjects

Diagnosis and Main Criteria for Inclusion:

Main Inclusion:

1. Male or female subject ≥ 18 years of age.
2. Subject had a clinical diagnosis of chronic plaque psoriasis (with a disease duration of at least 6 months) as determined by subject interview of his/her medical history and confirmation of diagnosis through physical examination by the Investigator.
3. Subject had at least one (1) fingernail with nail psoriasis and met 1 of the following criteria:
   - BSA ≥ 10% and a target fingernail modified Nail Psoriasis Severity Index (mNAPSI) ≥ 8 at Baseline, OR
   - BSA ≥ 5%, a target fingernail mNAPSI ≥ 8 and a total mNAPSI score of ≥ 20 at Baseline.
4. Subject had a Physician's Global Assessment of Fingernail Psoriasis (PGA-F) of at least moderate.
5. Subject had a Physician's Global Assessment of Skin Psoriasis (PGA-S) of at least moderate.
6. Subject had at least 1 of the following:
   - Nail Psoriasis Physical Functioning Severity score of > 3, OR
   - Nail Psoriasis Pain NRS score of > 3.
7. Subjects' target fingernail had an mNAPSI score of ≥ 8.

Main Exclusion:

1. Subjects had previous exposure to adalimumab (Humira®).
2. Subject was diagnosed with erythrodermic psoriasis generalized or localized pustular psoriasis, medication-induced or medication-exacerbated psoriasis, or new onset guttate psoriasis.
3. Subject was diagnosed with other active skin diseases or skin infections (bacterial, fungal, or viral) that may have interfered with evaluation of skin or fingernail psoriasis.
4. Subject was taking or required oral or injectable corticosteroids during the study. Inhaled corticosteroids for stable medical conditions were allowed.

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

Adalimumab 40 mg/0.8 mL via subcutaneous injection
Bulk Product Lot Numbers: 13-000648, 15-000609

Duration of Treatment: 52 weeks (last dose of adalimumab was received at Week 51)

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:

Placebo for adalimumab 0.8 mL via subcutaneous injection
Bulk Product Lot Numbers: 12-007038, 13-000828

Criteria for Evaluation

Efficacy:

The primary efficacy endpoint was the proportion of subjects achieving a total-fingernail mNAPSI 75 response, defined as at least a 75% reduction in total mNAPSI of all fingernails relative to Baseline at Week 26.

Ranked secondary efficacy endpoints in the order at which statistical analyses were conducted:

1. Percent change from Baseline in total NAPSI of all fingernails at Week 26.
2. Proportion of subjects achieving mNAPSI = 0 in all fingernails at Week 26.
3. Change from Baseline in Nail Psoriasis Pain Numeric Rating Scale (NRS) at Week 26.
4. Change from Baseline in Nail Psoriasis Physical Functioning Severity score at Week 26.
5. Proportion of subjects with at least 50% improvement in the scalp component of the Brigham Scalp Nail Inverse Palmo-Plantar Psoriasis Index (B-SNIPI) (among subjects with Baseline scalp score of 6 or greater) at Week 26.
6. Proportion of subjects achieving PGA-F of "clear" or "minimal" with at least a 2-grade improvement at Week 26.

For US regulatory purposes, the following primary endpoint and order of ranked secondary endpoints applied:

The primary efficacy endpoint was the proportion of subjects with PGA-F of "clear" or "minimal" with at least a 2-grade improvement at Week 26.

Ranked secondary efficacy endpoints in the order at which statistical analyses were conducted:

1. Proportion of subjects achieving a total-fingernail mNAPSI 75 response, defined as at least a 75% reduction in total mNAPSI of all fingernails relative to Baseline at Week 26.
2. Percent change from Baseline in total NAPSI of all fingernails at Week 26.
3. Proportion of subjects achieving mNAPSI = 0 in all fingernails at Week 26.
4. Change from Baseline in Nail Psoriasis Pain Numeric Rating Scale (NRS) at Week 26.
5. Change from Baseline in Nail Psoriasis Physical Functioning Severity score at Week 26.
6. Proportion of subjects with at least 50% improvement in the scalp component of the B-SNIPI (among subjects with Baseline scalp score of 6 or greater) at Week 26.

Other efficacy endpoints analyzed at each scheduled visit (except those included as primary or ranked secondary endpoints) were:

1. Proportion of subjects achieving a total-fingernail mNAPSI 75 response
2. Proportion of subjects achieving PGA-F of "clear" or "minimal"
3. Proportion of subjects achieving PGA-F of "clear"
4. Proportion of subjects achieving "clear" or "minimal" in nail bed component of the PGA-F, among those with Baseline nail bed component of "moderate" or worse

Criteria for Evaluation (Continued)

Efficacy (Continued):

5. Proportion of subjects achieving "clear" or "minimal" in nail matrix component of the PGA-F, among those with Baseline nail matrix component of "moderate" or worse
6. Proportion of subjects achieving mNAPSI = 0 of the target fingernail
7. Proportion of subjects achieving mNAPSI = 0 of all fingernails
8. Proportion of subjects achieving mNAPSI ≤ 2 of the target fingernail
9. Proportion of subjects achieving mNAPSI ≤ 2 of all fingernails
10. Change and percent change from Baseline in mNAPSI of the target fingernail
11. Change and percent change from Baseline in mNAPSI of the all fingernails
12. Proportion of subjects achieving NAPSI = 0 in all fingernails
13. Proportion of subjects achieving NAPSI = 0 in target fingernail
14. Change and percent change from Baseline in NAPSI of the target fingernail
15. Change and percent change from Baseline in NAPSI of the all fingernails
16. Change and percent change from Baseline in Psoriasis Area Severity Index (PASI)
17. Proportion of subjects achieving PASI 75/50/90/100 among subjects with Baseline PASI ≥ 5
18. Proportion of subjects achieving PGA-S of "clear" or "minimal"
19. Proportion of subjects achieving PGA-S of "clear"
20. Proportion of subjects achieving 50% improvement in the scalp component of the B-SNIPI (among subjects with Baseline scalp score of 6 and greater)
21. Proportion of subjects achieving 50% improvement in the inverse psoriasis component of the B-SNIPI (among subjects with Baseline inverse psoriasis score of 6 and greater)
22. Change and percent change from Baseline in BSA
23. Change and percent change from Baseline in Nail Psoriasis Pain NRS
24. Change and percent change from Baseline in Nail Psoriasis Physical Functioning Severity
25. Change and percent change from Baseline in Nail Assessment in Psoriasis and Psoriatic Arthritis Quality of Life (NAPPA QoL)
26. Change from Baseline in Dermatology Life Quality Index (DLQI)
27. Proportion of subjects achieving DLQI of 0, and achieving DLQI of 0/1
28. Change from Baseline in Work Productivity and Activity Impairment Nail Psoriasis (WPAI: NPSO)
29. Change from Baseline in European Quality of Life – 5 Dimensions (EQ-5D) Health Status Assessment
30. Change from Baseline in Hospital Anxiety Depression Scale (HADS)
31. Proportion of subjects with a new diagnosis of psoriatic arthritis (PsA) during the study (with adverse event of PsA) among subjects without PsA at Baseline
32. Change from Baseline in Nail Psoriasis Quality of Life (Nail Psoriasis QoL)

Criteria for Evaluation (Continued)

Pharmacokinetic:

Blood samples were collected for the measurement of serum adalimumab concentrations at Baseline and Weeks 4, 8, 12, 16, 25, 26, 36, 51, and 52, or at the Premature Discontinuation visit if the subject discontinued prior to Week 52. Blood samples were collected for the measurement of serum anti-adalimumab antibody (AAA) at Baseline, Weeks 4, 8, 12, 16, 25, 26, 36, 51, and 52, or at the Premature Discontinuation visit if the subject discontinued prior to Week 52.

Safety:

Safety analyses were performed on all subjects who received at least 1 dose of study drug. Incidence of adverse events (AEs), changes in vital signs, physical examination results, and clinical laboratory tests (hematology, chemistry, and urinalysis) were assessed.

Statistical Methods

Efficacy:

The efficacy analysis was conducted in the ITT Population in Period A (ITT_A Population), defined as all subjects randomized at Baseline. All efficacy variables were also summarized in the ITT_B Population (all subjects who received at least 1 dose of study drug in Period B), as well as the ADA_EOW Population (all subjects who were randomized to adalimumab at Week 0) to evaluate the efficacy of long-term treatment.

The primary analysis was the comparison of the adalimumab treatment group versus the placebo treatment group in the primary endpoint, proportion of subjects achieving mNAPSI 75 at Week 26, with the exception that for US regulatory purposes, the primary endpoint was the proportion of subjects achieving PGA-F of "clear" or "minimal" with at least a 2-grade improvement at Week 26.

The primary efficacy analysis was carried out in the ITT_A Population. Multiple imputation (MI) was used as the primary approach to impute the missing values, with non-responder imputation (NRI) as sensitivity analysis for the primary endpoint. The primary efficacy endpoint was analyzed using a Cochran-Mantel-Haenszel (CMH) test, stratified by pooled center (due to large number of centers included in the study, centers were combined according to the rank order of center size).

For the other efficacy analyses, categorical variables were analyzed using CMH test with the pooled center as a stratification factor, and continuous variables were analyzed using analysis of covariance (ANCOVA) method, with treatment, pooled center, and Baseline value in the model.

For the ITT_B Population, results were calculated separately for subjects who were randomized to placebo in Period A (PBO/EOW) and for subjects who were randomized to adalimumab eow in Period A (EOW/EOW), although statistical comparisons were not made between the 2 treatment groups. Missing data were imputed using NRI and/or last observation carried forward (LOCF). In the summaries for the ADA_EOW Population, MI, NRI and LOCF methods of imputation were used.

Pharmacokinetic:

Adalimumab trough serum concentrations were summarized by treatment group at each time point using descriptive statistics. In addition, PK model based analyses were performed with the focus on apparent clearance (CL/F) and apparent volume of distribution (V/F) of adalimumab. AAA was evaluated for each subject and each regimen, and rates of AAA positive were calculated for Period A. The effect of AAA on adalimumab pharmacokinetics, efficacy variable(s), and treatment-emergent AEs were evaluated.

Statistical Methods (Continued)

Safety:

All AEs, serious adverse events (SAE), AEs leading to discontinuation, and pre-specified AEs of special interest were collected during the study and up to 70 days after the last dose of study drug. Safety analyses were performed using the Safety Population in each period (subjects who received at least 1 dose of study drug in each period) and the All Adalimumab Treated Population (subjects who received at least 1 dose of adalimumab in the study). A list of pretreatment SAEs was provided. A treatment-emergent AE was defined as an event with onset or worsening after the first dose of study drug and within 70 days after the last dose of study drug. The number and percent of subjects experiencing treatment-emergent AEs were tabulated using the Medical Dictionary for Drug Regulatory Activities (MedDRA®) Version 18.0 system organ class and preferred term. Comparisons of the percentages of subjects experiencing an AE in the adalimumab group versus the placebo group were performed using Fisher's exact tests for data collected in Period A. Summaries (including percentages and events per 100 patient-years) of SAEs, deaths, AEs leading to discontinuation from the study, and pre-specified AEs of special interest were provided as well. Mean change in laboratory variables and vital sign variables at each visit were summarized for all treated subjects; the comparison between the adalimumab treatment group and placebo group was carried out in Period A using a 1-way ANOVA. For selected parameters, a listing of all subjects with any laboratory determination meeting Common Toxicity Criteria (CTC) of Grade 3 or higher was provided. Shift tables for changes from Baseline according to the normal range were also provided.

Summary/Conclusions

Efficacy Results:

Study M13-674 evaluated the safety and efficacy of adalimumab, as compared with placebo, for the treatment of nail psoriasis in adult subjects with chronic plaque psoriasis.

In Period A, a total of 217 subjects were randomized 1:1 to either placebo (N = 108) or adalimumab 40 mg eow (N = 109) and comprise the ITT_A Population. The majority of subjects in the ITT_A Population were male and white. The mean BMI was approximately 30 kg/m^2 and the mean age was approximately 47 years. Baseline demographic and disease characteristics were consistent with the intended subject population and were generally balanced between the two treatment groups. The median duration of psoriasis was approximately 16 years and the median duration of fingernail psoriasis was approximately 9 years.

All randomized subjects in Period A received at least 1 dose of study drug. There were 94 subjects in the placebo group and 94 subjects from the adalimumab eow group who completed Period A (either continued to Week 26 or early escaped to Week 26 per protocol requirement) and entered Period B. Fewer subjects in the adalimumab eow group early escaped to Week 26 (8 subjects in the adalimumab eow group versus 56 subjects in the placebo group). The most frequently reported primary reasons for discontinuation were due to an AE (8 subjects; 5 subjects in the adalimumab eow group versus 3 subjects in the placebo group) or withdrawal of consent (7 subjects; 4 subjects in the adalimumab eow group versus 3 subjects in the placebo group). All 188 subjects who entered Period B were treated with adalimumab eow. Of these 188 subjects, 168 (89.4%) completed Period B. Of the 20 subjects who discontinued prematurely from Period B, 13 had been randomized to placebo in Period A (PBO/EOW) and 7 had been randomized to adalimumab (EOW/EOW). Six PBO/EOW subjects and 4 EOW/EOW subjects discontinuation from Period B primarily due to lack of efficacy. No subjects discontinued from Period B due to adverse events.

Summary/Conclusions (Continued)

Efficacy Results (Continued):

All primary and ranked secondary efficacy endpoints achieved clinically meaningful and highly statistically significant differences and are presented as follows:

Period A							
Rank	**US Rank**	**Secondary Variable**	**PBO**	**ADA eow**	**Difference**	**(95% CI)**	***P* value**
Primary	1	Proportion of subjects achieving a total fingernail mNAPSI 75 response at Week 26 (%)	3.4	46.6	43.2	(32.8, 53.6)[a]	< 0.001[b]***
6	Primary	Proportion of subjects achieving PGA-F of "clear" or "minimal" with a 2-grade improvement at Week 26 (%)	6.9	48.9	42.0	(30.8, 53.2)[a]	< 0.001[b]***
1	2	Percent change from Baseline in total fingernail NAPSI at Week 26 (LS Mean)	–11.5	–56.2	–44.8	(–53.5, –36.0)	< 0.001[c]***
2	3	Proportion of subjects achieving total fingernail mNAPSI = 0 at Week 26 (%)	0	6.6	6.6	(1.8, 11.3)[a]	0.008[b]**
3	4	Change from Baseline in Nail Psoriasis Pain NRS at Week 26 (LS Mean)	–1.1	–3.7	–2.6	(–3.3, –2.0)	< 0.001[c]***
4	5	Change from Baseline in Nail Psoriasis Physical Functioning Severity score at Week 26 (LS Mean)	–0.8	–3.7	–2.9	(–3.6, –2.2)	< 0.001[c]***
5	6	Proportion of subjects with at least 50% improvement in the scalp component of the B-SNIPI (among subjects with Baseline scalp score of 6 or greater) at Week 26 (%)[d]	0.4	58.3	57.9	(33.8, 82.0)[a]	0.002[b]**

ADA = adalimumab; B-SNIPI = Brigham Scalp Nail Inverse Palmo-Plantar Psoriasis Index; CI = confidence interval; eow = every other week; LS = least square; mNAPSI = Modified Nail Psoriasis Severity Index; NAPSI = Nail Psoriasis Severity Index; NRS = numeric rating scale; PGA-F = Physician's Global Assessment of Fingernails

a. Across all strata, 95% CI for adjusted difference was calculated according to the extended Mantel-Haenszel statistic for the comparison of 2 treatment groups. If zero frequency occurred, strata were dropped and 95% CI for difference was calculated based on normal approximation to the binomial distribution.

Summary/Conclusions (Continued)

Efficacy Results (Continued):

b. Across all the strata, *P* value was calculated based on student's T-distribution from PROC MIANALYZE procedure according to the Cochran-Mantel-Haenszel test adjusted for strata using Wilson-Hilferty transformation. If zero frequency occurred, strata were dropped and *P* value was calculated based on Chi-square test (or adjusted Chi-square test based on Campbell [2007] if expected count < 5 in any cell).

c. Across all the strata, *P* value was calculated from ANCOVA with stratum, Baseline value, and treatment in the model.

d. For subjects enrolled under protocol amendment 1 in the US and Puerto Rico only (placebo n = 12 and ADA eow n = 18).

Note: ** and *** denote P ≤ 0.01 and ≤ 0.001, respectively.

Results of the other secondary endpoints support the primary efficacy endpoint results. Key other secondary efficacy endpoints are as follows:

- Results for the target fingernail mNAPSI were similar to the total fingernail mNAPSI with a higher mNAPSI 75 response rate at Week 26 and greater mean decreases in target mNAPSI score from Baseline to Week 26 in the adalimumab eow group than in the placebo group.
- At Week 26, the mean percent decrease from Baseline in PASI was greater for subjects in the adalimumab eow group compared with subjects in the placebo group. Additionally, a higher proportion of subjects in the adalimumab eow group achieved PASI 75, PASI 90, and PASI 100 at Week 26 in Period A compared with subjects in the placebo group.
- Results for the PGA-S were similar to those for the PGA-F with a higher proportion of subjects in the adalimumab eow group achieving a PGA-S of "clear" or "minimal" with at least a 2-grade improvement from Baseline at Week 26 compared with placebo.
- Mean improvements in Nail Psoriasis QoL score and NAPPA QoL score were larger for subjects in the adalimumab eow group compared with subjects in the placebo group.

For subjects who continued in the study to Period B, improvement in efficacy and quality of life measures observed in the adalimumab eow treatment group in 26 weeks of treatment in Period A was maintained or increased through Week 52 in Period B. Subjects who were randomized to placebo in Period A improved and in most measures achieved similar results by Week 52 when switched to eow adalimumab in Period B as adalimumab subjects did at the end of Period A. Additionally, the proportion of subjects with complete resolution of symptoms (total fingernail mNAPSI = 0 and NAPSI = 0) was higher at Week 52 among subjects who had been receiving adalimumab since Baseline (EOW/EOW) (20.2% for both total fingernail mNAPSI = 0 and NAPSI = 0) than among subjects who had been receiving adalimumab for only 26 weeks in Period B (PBO/EOW) (11.7% for both total fingernail mNAPSI = 0 and NAPSI = 0).

Key efficacy endpoints in Period B are summarized in the following table.

Summary/Conclusions (Continued)
Efficacy Results (Continued):

	Period B			
		PBO/EOW		EOW/EOW
Variable	**N**		**N**	
Proportion of subjects achieving total fingernail mNAPSI 75 – NRI, n (%)				
Entry into Period B	94	5 (5.3%)	94	46 (48.9%)
At Week 52	94	47 (50.0%)	94	53 (56.4%)
Proportion of subjects achieving a PGA-F of "clear" or "minimal" with at least a 2-grade improvement from Baseline – NRI, n (%)				
Entry into Period B	94	5 (5.3%)	94	47 (50.0%)
At Week 52	94	50 (53.2%)	94	50 (53.2%)
Percent change from Baseline in total fingernail NAPSI (LS Mean) – LOCF				
At entry into Period B	94	–8.8	94	–57.3
At Week 52	88	–67.4	90	–68.3
Proportion of subjects achieving total fingernail mNAPSI = 0 – NRI, n (%)				
At entry to Period B	94	0	94	7 (7.4)
At Week 52	94	11 (11.7)	94	19 (20.2)
Change from Baseline in Nail Ps Pain NRS (LS Mean) – LOCF				
At entry into Period B	94	–1.1	94	–3.7
At Week 52	94	–3.6	93	–4.1
Change from Baseline in Nail Ps Physical Functioning Severity score (LS Mean) – LOCF				
At entry into Period B	94	–0.6	94	–3.7
At Week 52	94	–3.4	93	–3.9
Proportion of subjects with at least 50% improvement in the scalp component of the B-SNIPI – NRI, n (%)				
At entry into Period B	9	0	16	10 (62.5)
At Week 52	9	4 (44.4)	16	11 (68.8)

Summary/Conclusions (Continued)
Efficacy Results (Continued):

	Period B			
		PBO/EOW		EOW/EOW
Variable	**N**		**N**	
Proportion of subjects achieving PASI improvement of at least 75% relative to Baseline (%) – NRI, n (%)				
At entry into Period B	83	10 (12.0)	84	58 (69.0)
At Week 52	83	56 (67.5)	84	56 (66.7)
Proportion of subjects achieving PASI improvement of at least 90% relative to Baseline (%) – NRI, n (%)				
At entry into Period B	83	5 (6.0)	84	43 (51.2)
At Week 52	83	35 (42.2)	84	39 (46.4)
Proportion of subjects achieving PASI improvement of 100% relative to Baseline (%) – NRI, n (%)				
At entry into Period B	83	1 (1.2)	84	25 (29.8)
At Week 52	83	23 (27.7)	84	26 (31.0)
Proportion of subjects achieving PGA-S of "clear" or "minimal" with at least a 2-grade improvement relative to Baseline (%) – NRI, n (%)				
At entry into Period B	94	8 (8.5)	94	63 (67.0)
At Week 52	94	56 (59.6)	94	50 (53.2)

PBO/EOW: subjects randomized to placebo in Period A and receiving at least 1 dose of adalimumab in Period B; EOW/EOW: subjects randomized to adalimumab every other week in Period A and receiving at least 1 dose of adalimumab in Period B

LOCF = last observation carried forward; LS mean = least squares mean; mNAPSI = Modified Nail Psoriasis Severity Index; NRI = non-responder imputation; PASI = Psoriasis Area Severity Index; PGA-F = Physician's Global Assessment of Fingernail Psoriasis; PGA-S = Physician's Global Assessment of Skin Psoriasis

Summary/Conclusions (Continued)

Efficacy Results (Continued):

Efficacy results were also summarized in the ADA_EOW Population, which included all subjects who were randomized to adalimumab eow at Week 0. Results demonstrate the maintenance of efficacy through Week 52 for most endpoints. NAPSI and mNAPSI results showed continuous improvement through Week 52. PGA-F, PGA-S, Nail Psoriasis Pain NRS, PASI and Nail Psoriasis Physical Functioning Severity scores tended to plateau at Week16 to Week 26 and remained stable through Week 52. The proportion of subjects achieving 50%, 75%, or 100% improvement in B-SNIPI scores (scalp and inverse psoriasis components) generally peaked or plateaued at Week 16 or Week 26.

Pharmacokinetic Results:

PK and immunogenicity results and conclusions are presented in a separate report.

Safety Results:

In Study M13-674, adalimumab was generally safe and well tolerated as evaluated by treatment-emergent adverse events (TEAEs), laboratory values, and vital signs values. During Period A, the proportions of subjects with any AE, including SAEs, were generally comparable between adalimumab and placebo treatment groups. The most common AEs among all adalimumab-treated subjects, including nasopharyngitis and upper respiratory tract infection, are expected for this population of subjects with chronic plaque psoriasis, and are comparable to the proportions of subjects who have been noted to experience these AEs in other adalimumab clinical trials. The majority of TEAEs were considered by the Investigator to be mild or moderate in severity and as having no reasonable possibility of being related to study drug. The rates of study drug discontinuation due to TEAEs were relatively balanced across treatment groups in Period A and no AEs led to discontinuation in Period B. No deaths or malignancies were reported in this study. Nine infectious SAEs were reported in 7 subjects treated with adalimumab. No opportunistic infections were reported.

No clinically meaningful changes in laboratory parameters or vital signs were noted in adalimumab-treated subjects.

Overall, the safety profile of adalimumab treatment observed in this study is expected given the population of subjects with chronic plaque psoriasis, and is consistent with the experience in other adalimumab clinical trials.

Conclusions:

Adalimumab 40 mg eow was superior to placebo in the treatment of nail psoriasis in adult patients with chronic plaque psoriasis as demonstrated by the primary endpoints and supported by the ranked secondary endpoints. Efficacy results were maintained during long-term treatment of up to 52 weeks with adalimumab. No new safety signals were identified. The clinical data from this study support the assertion that the benefits outweigh the known risks of adalimumab treatment, as administered in this study.