FINAL CLINICAL STUDY REPORT

Study Title:	Combined Phase 2b/3, Double-Blind, Randomized, Placebo-Controlled Studies Evaluating the Efficacy and Safety of Filgotinib in the Induction and Maintenance of Remission in Subjects with Moderately to Severely Active Ulcerative Colitis
Name of Test Drug:	Filgotinib (GS-6034, formerly GLPG0634)
Dose and Formulation:	Filgotinib 100-mg and 200-mg tablets
Indication:	Ulcerative Colitis
Sponsor:	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA
Study No.:	GS-US-418-3898 (SELECTION)
Phase of Development:	Phase 2b/3
IND No.: **EudraCT No.:**	129647 2016-001392-78
ClinicalTrials.gov Identifier:	NCT02914522
Study Start Date:	14 November 2016 (First Subject Screened)
Study End Date:	31 March 2020 (Last Subject Last Observation for the Primary Endpoint)
Principal or Coordinating Investigator:	Name: PPD Affiliation: Department of Gastroenterology, PPD
Gilead Responsible Medical Monitor:	Name: PPD Telephone: PPD Fax: PPD
Report Date:	10 August 2020

CONFIDENTIAL AND PROPRIETARY INFORMATION

This study was conducted in accordance with the guidelines of Good Clinical Practice, including archiving of essential documents.

STUDY SYNOPSIS

Study GS-US-418-3898
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
USA

Title of Study: Combined Phase 2b/3, Double-Blind, Randomized, Placebo-Controlled Studies Evaluating the Efficacy and Safety of Filgotinib in the Induction and Maintenance of Remission in Subjects with Moderately to Severely Active Ulcerative Colitis

Investigators: Multicenter study

Study Centers: This study was conducted at 341 study centers in 40 countries: Argentina, Australia, Austria, Belgium, Bulgaria, Canada, Croatia, Czech Republic, France, Germany, Greece, Hong Kong, Hungary, India, Ireland, Israel, Italy, Japan, Malaysia, Mexico, Netherlands, New Zealand, Norway, Poland, Portugal, Republic of Georgia, Republic of Korea, Romania, Russian Federation, Serbia, Singapore, Slovakia, South Africa, Spain, Sweden, Switzerland, Taiwan, Ukraine, United Kingdom, and the United States.

Publications: There were no publications at the time of this CSR.

Study Period:

14 November 2016 (First Subject Screened)
31 March 2020 (Last Subject Last Observation for the Primary Endpoint)

Phase of Development: Phase 2b/3

Objectives:

Induction Studies: Cohort A (Biologic Naive) and Cohort B (Biologic Experienced)

The primary objective of the induction studies was as follows:

- To evaluate the efficacy of filgotinib as compared with placebo in establishing endoscopy/bleeding/stool frequency (EBS) remission at Week 10

The secondary objectives of the induction studies were as follows:

- To evaluate the efficacy of filgotinib as compared with placebo in establishing Mayo Clinic Score (MCS) remission at Week 10
- To evaluate the efficacy of filgotinib as compared with placebo in establishing an endoscopic subscore of 0 at Week 10
- To evaluate the efficacy of filgotinib as compared with placebo in establishing Geboes histologic remission at Week 10

- To evaluate the efficacy of filgotinib as compared with placebo in establishing MCS remission (alternative definition) at Week 10
- To evaluate the safety and tolerability of filgotinib
- To assess the pharmacokinetic (PK) characteristics of filgotinib

Maintenance Study:

The primary objective of the Maintenance Study was as follows:

- To evaluate the efficacy of filgotinib as compared with placebo in establishing EBS remission at Week 58

The secondary objectives of the Maintenance Study were as follows:

- To evaluate the efficacy of filgotinib as compared with placebo in establishing MCS remission at Week 58
- To evaluate the efficacy of filgotinib as compared with placebo in establishing sustained EBS remission at Week 58, defined as EBS remission at Weeks 10 and 58
- To evaluate the efficacy of filgotinib as compared with placebo in establishing 6-month corticosteroid-free EBS remission at Week 58
- To evaluate the efficacy of filgotinib as compared with placebo in establishing an endoscopic subscore of 0 at Week 58
- To evaluate the efficacy of filgotinib as compared with placebo in establishing Geboes histologic remission at Week 58
- To evaluate the efficacy of filgotinib as compared with placebo in establishing MCS remission (alternative definition) at Week 58
- To evaluate the safety and tolerability of filgotinib
- To assess the PK characteristics of filgotinib

Methodology: These were combined Phase 2b/3 double-blind, randomized, placebo-controlled studies evaluating the efficacy and safety of filgotinib in the induction and maintenance of remission in subjects with moderately to severely active ulcerative colitis (UC).

Blinded Induction Studies (Day 1 to Week 11):

Subjects who provided written consent and met all eligibility criteria were enrolled into either the Cohort A (Biologic Naive) Induction Study or Cohort B (Biologic Experienced) Induction Study and subsequently randomized in a blinded fashion in a 2:2:1 ratio to receive 1 of 3 treatments as follows:

Filgotinib 200 mg: filgotinib 200 mg + placebo to match (PTM) filgotinib 100 mg, once daily

Filgotinib 100 mg: filgotinib 100 mg + PTM filgotinib 200 mg, once daily

Placebo: PTM filgotinib 200 mg + PTM filgotinib 100 mg, once daily

Note: US and Korea males who had not failed at least 2 biologic therapies (any tumor necrosis factor [TNF]-α antagonist and vedolizumab; non-dual refractory) were randomized in a 2:1 ratio to either filgotinib 100 mg or respective placebo.

Subjects who were biologic naive in the Cohort A Induction Study were stratified based on the following factors:

- Concomitant use of oral, systemic corticosteroids (eg, prednisone) at Day 1 (Yes or No)
- Concomitant use of immunomodulators (eg, 6-mercaptopurine [6-MP], azathioprine, methotrexate [MTX]) at Day 1 (Yes or No)

Subjects who were biologic experienced in the Cohort B Induction Study were stratified based on the following factors:

- Exposure to one biologic agent versus more than one biologic agent
- Concomitant use of oral, systemic corticosteroids (eg, prednisone) at Day 1 (Yes or No)
- Concomitant use of immunomodulators (eg, 6-MP, azathioprine, MTX) at Day 1 (Yes or No)

At Week 10, efficacy assessments for EBS remission and MCS response were performed. Subjects continued on their assigned treatment in a blinded fashion through the end of Week 10 until rerandomization at Week 11.

At Week 11, subjects who completed the Cohort A Induction Study or Cohort B Induction Study and achieved either EBS remission or MCS response at Week 10 were rerandomized into the Maintenance Study. Subjects who achieved neither EBS remission nor MCS response at Week 10 had the option to enter a separate, long-term extension (LTE) study (GS-US-418-3899).

Subjects who met disease worsening criteria in the Maintenance Study were discontinued from blinded treatment and offered the option to receive open-label filgotinib in the LTE study.

Blinded Maintenance Study (Week 11 to Week 58):

Subjects in the Maintenance Study were stratified based on the following factors:

- Participation in Cohort A or Cohort B
- Concomitant use of oral, systemic corticosteroids (eg, prednisone) at Day 1 (Yes or No)
- Concomitant use of immunomodulators (eg, 6-MP, azathioprine, MTX) at Day 1 (Yes or No)

Subjects from the Cohort A and Cohort B Induction Studies who were eligible for the Maintenance Study were rerandomized to treatment as follows:

Treatment Assignment in Induction Studies: Cohorts A and B	**Maintenance Study Rerandomization:**
Filgotinib 200 mg	Filgotinib 200 mg
	Placebo
Filgotinib 100 mg	Filgotinib 100 mg
	Placebo
Placebo	Placebo

Subjects who received either filgotinib 200 mg or filgotinib 100 mg in the induction studies were randomized in a 2:1 manner to either continue on the assigned filgotinib regimen or switch to placebo for the duration of the Maintenance Study.

Subjects who withdrew from the study completed early termination, followed by posttreatment assessments 30 days after the last dose of study drug.

Subjects who completed the Week 58 visit had the option to continue study drug in a blinded fashion in the LTE study.

Number of Subjects (Planned and Analyzed):
Planned: 1300 subjects (650 subjects each for Cohorts A and B)
Analyzed by Analysis Set:

Cohort A Induction Study

	Filgotinib 200 mg (N=245)	Filgotinib 100 mg (N=278)	Placebo (N=137)	Total (N=660)
All Randomized Analysis Set	245 (100.0%)	278 (100.0%)	137 (100.0%)	660 (100.0%)
Safety Analysis Set	245 (100.0%)	277 (99.6%)	137 (100.0%)	659 (99.8%)
Full Analysis Set	245 (100.0%)	277 (99.6%)	137 (100.0%)	659 (99.8%)
Per-Protocol Analysis Set	235 (95.9%)	253 (91.0%)	125 (91.2%)	613 (92.9%)
Biomarker Analysis Set	244 (99.6%)	271 (97.5%)	137 (100.0%)	652 (98.8%)
PK Analysis Set	242 (98.8%)	263 (94.6%)	0	505 (76.5%)
PK Substudy Analysis Set	4 (1.6%)	11 (4.0%)	0	15 (2.3%)

PK pharmacokinetic

Cohort B Induction Study

	Filgotinib 200 mg (N=262)	Filgotinib 100 mg (N=286)	Placebo (N=143)	Total (N=691)
All Randomized Analysis Set	262 (100.0%)	286 (100.0%)	143 (100.0%)	691 (100.0%)
Safety Analysis Set	262 (100.0%)	285 (99.7%)	142 (99.3%)	689 (99.7%)
Full Analysis Set	262 (100.0%)	285 (99.7%)	142 (99.3%)	689 (99.7%)
Per-Protocol Analysis Set	235 (89.7%)	251 (87.8%)	123 (86.0%)	609 (88.1%)
Biomarker Analysis Set	262 (100.0%)	285 (99.7%)	142 (99.3%)	689 (99.7%)
PK Analysis Set	249 (95.0%)	271 (94.8%)	0	520 (75.3%)
PK Substudy Analysis Set	9 (3.4%)	17 (5.9%)	0	26 (3.8%)

PK pharmacokinetic

Maintenance Study

	Induction Filgotinib 200 mg		Induction Filgotinib 100 mg		Induction Placebo	
	Maintenance Filgotinib 200 mg (N=202)	Maintenance Placebo (N=99)	Maintenance Filgotinib 100 mg (N=179)	Maintenance Placebo (N=91)	Maintenance Placebo (N=93)	Overall Total (N=664)
All Randomized Analysis Set	202 (100.0%)	99 (100.0%)	179 (100.0%)	91 (100.0%)	93 (100.0%)	664 (100.0%)
Safety Analysis Set	202 (100.0%)	99 (100.0%)	179 (100.0%)	91 (100.0%)	93 (100.0%)	664 (100.0%)
PK Analysis Set	173 (85.6%)	0	136 (76.0%)	0	0	309 (46.5%)
Full Analysis Set	199 (98.5%)	98 (99.0%)	172 (96.1%)	89 (97.8%)	—	558 (97.7%)
Per-Protocol Analysis Set	179 (88.6%)	87 (87.9%)	151 (84.4%)	75 (82.4%)	—	492 (86.2%)
Biomarker Analysis Set	199 (98.5%)	97 (98.0%)	170 (95.0%)	87 (95.6%)	—	553 (96.8%)

PK pharmacokinetic

Diagnosis and Main Criteria for Inclusion:

Main Eligibility Criteria for the Induction Studies (Cohorts A & B):

Eligible subjects met all of the following inclusion criteria for participation in the Cohort A or Cohort B Induction Studies:

- Males or nonpregnant, nonlactating females, ages 18 to 75 years, inclusive based on the date of the screening visit
- Documented diagnosis of UC of at least 6 months and with a minimum disease extent of 15 cm from the anal verge
- Moderately to severely active UC as determined by a centrally read endoscopy score ≥ 2, a rectal bleeding score ≥ 1, a stool frequency score ≥ 1, and Physician's Global Assessment of ≥ 2 as determined by the Mayo Clinic scoring system with endoscopy occurring during screening; total score between 6 and 12, inclusive
- A surveillance colonoscopy was required prior to screening in subjects with a history of UC for 8 or more years, if one was not performed in the prior 24 months
- Subjects may have been on a stable dose of the following: oral 5-aminosalicylate (5-ASA) compounds, azathioprine, 6-MP, or MTX (dose must have been stable 4 weeks prior to randomization through 10 weeks after randomization); oral corticosteroid therapy (prednisone prescribed at a stable dose ≤ 30 mg/day or budesonide prescribed at a stable dose of ≤ 9 mg/day, prescribed dose must have been stable for 2 weeks prior to randomization through 14 weeks after randomization)
- Must not have had Crohn's disease, indeterminate colitis, ischemic colitis, fulminant colitis, isolated ulcerative proctitis, or toxic mega-colon
- Must not have had active tuberculosis (TB) or history of latent TB that had not been treated

Additional Eligibility Criteria for Cohort A (Biologic Naive) Induction Study:

- Previously demonstrated an inadequate clinical response, loss of response to, or intolerance to at least one of the following agents (depending on current country treatment recommendations/guidelines):

  Corticosteroids: active disease despite a history of at least an induction regimen of a dose equivalent to oral prednisone 30 mg daily for 2 weeks or intravenously (IV) for 1 week, or 2 failed attempts to taper steroids below a dose equivalent of 10 mg daily prednisone, or a history of steroid intolerance

  Immunomodulators: active disease despite a history of at least a 12-week regimen of oral azathioprine (≥ 2 mg/kg/day) or 6-MP (≥ 1 mg/kg/day), or MTX (25 mg subcutaneously [SC] or intramuscularly [IM] per week for induction and ≥ 15 mg IM per week for maintenance), or a history of intolerance to at least one immunomodulator

- No prior or current use of any TNF-α antagonist
- No prior or current use of vedolizumab at any time

Additional Eligibility Criteria for Cohort B (Biologic Experienced) Induction Study:

- Previously demonstrated an inadequate clinical response, loss of response to, or intolerance of at least one of the following agents (depending on current country treatment recommendations/guidelines):

  TNF-α Antagonists: active disease despite a history of at least one induction regimen of a TNF-α antagonist: infliximab (minimum induction regimen of 5 mg/kg at 0, 2, and 6 weeks [in the European Union (EU), duration of treatment of 14 weeks]); adalimumab (8-week induction regimen consisting of 160 mg [four 40-mg injections in 1 day or two 40-mg injections per day for 2 consecutive days] on Day 1, followed by a second dose 2 weeks later of 80 mg and a 40-mg dose 2 weeks later, followed by a 40-mg dose every other week until Week 8); golimumab (minimum induction duration of 6 weeks [12 weeks in EU] including a 200 mg SC injection at Week 0, followed by 100 mg at Week 2, and then 100 mg every 4 weeks), or a recurrence of symptoms during maintenance therapy with any of these agents, or a history of intolerance to any TNF-α antagonists

  Vedolizumab: active disease despite a history of at least a 14-week (10 weeks in EU) induction regimen consisting of 300 mg IV at Weeks 0, 2, and 6, or a history of intolerance to vedolizumab

- Must not have used any TNF-α antagonist or vedolizumab ≤ 8 weeks prior to screening or any other biologic agent ≤ 8 weeks prior to screening or within 5 times the half-life of the biologic agent prior to screening, whichever was longer

Main Eligibility Criteria for Maintenance Study:

Subjects must have completed the Cohort A or Cohort B Induction Study with an MCS response or EBS remission based on Week 10 assessments.

Duration of Treatment: Up to 11 weeks for induction and up to 47 weeks for maintenance, for a total treatment duration of up to 58 weeks

Test Product, Dose, Mode of Administration, and Batch No.:

Filgotinib 200-mg tablet + PTM filgotinib 100-mg tablet, administered orally once daily

Filgotinib 100-mg tablet + PTM filgotinib 200-mg tablet, administered orally once daily

Filgotinib 100-mg tablet, administered orally once daily (non-dual refractory US/Korea males)

Batch Numbers:

- Filgotinib 200-mg tablets: EV1602D1, EV1609D1, EV1610D1, EV1613D1, EV1614D1, EV1709B1, EV1711B1, EV1715B1, EV1812B1
- Filgotinib 100-mg tablets: EV1602C1, EV1608C1, EV1609C1, EV1614C1, EV1702C1, EV1708B1, EV1710B1
- PTM filgotinib 200-mg tablets: EV1603D1, EV1612B1, EV1704B1, EV1705B2, EV1713B1, EV1809B1
- PTM filgotinib 100-mg tablets: EV1603C1, EV1611B1, EV1703B1, EV1808B1

Reference Therapy, Dose, Mode of Administration, and Batch No.:

PTM filgotinib 200-mg tablet + PTM filgotinib 100-mg tablet, administered orally once daily

PTM filgotinib 100-mg tablet, administered orally once daily (non-dual refractory US/Korea males)

Batch Numbers:

- PTM filgotinib 200-mg tablets: EV1603D1, EV1612B1, EV1704B1, EV1705B2, EV1713B1, EV1809B1
- PTM filgotinib 100-mg tablets: EV1603C1, EV1611B1, EV1703B1, EV1808B1

Criteria for Evaluation:

Efficacy: The primary efficacy endpoints were the proportion of subjects achieving EBS remission at Week 10 for the induction studies and at Week 58 for the Maintenance Study.

Key secondary efficacy endpoints for the induction studies were the proportion of subjects who achieved MCS remission at Week 10, the proportion of subjects who achieved an endoscopic subscore of 0 at Week 10, the proportion of subjects who achieved Geboes histologic remission at Week 10, and the proportion of subjects who achieved MCS remission (alternative definition) at Week 10.

Key secondary efficacy endpoints for the Maintenance Study were the proportion of subjects who achieved MCS remission at Week 58, the proportion of subjects who achieved sustained EBS remission, the proportion of subjects who achieved 6-month corticosteroid-free EBS remission at Week 58, the proportion of subjects who achieved endoscopic subscore of 0 at Week 58, the proportion of subjects who achieved Geboes histologic remission at Week 58, and the proportion of subjects who achieved MCS remission (alternative definition) at Week 58.

Additional exploratory endpoints included the proportion of subjects who achieved novel histologic outcomes at Week 10/Week 58, the proportion of subjects who achieved endoscopic response at Week 10/Week 58, the proportion of subjects who achieved MCS response at Week 10/Week 58, the proportion of subjects who achieved EBS remission (alternative definition) at Week 10/Week 58, proportion of subjects who achieved sustained MCS remission, the proportion of subjects who achieved 6-month corticosteroid-free MCS remission at Week 58, change from baseline in MCS and partial MCS at Week 10/Week 58, and change from baseline in health related quality of life (HRQoL) scores at Week 10/Week 58.

Pharmacokinetics/Pharmacodynamics: Plasma concentrations of filgotinib and GS-829845 (primary metabolite of filgotinib) were determined using validated bioanalytical assays.

Blood samples for pharmacokinetic (PK) analyses were collected at Week 4 (at least 30 minutes and up to 3 hours after study drug dosing), Week 10 (within 2 hours prior to dosing), Week 26 (without regard to dosing), and Week 58 (within 2 hours prior to dosing).

Steady-state PK was determined for subjects who participated in the optional PK substudy. Subjects in the PK substudy had additional plasma PK samples at any single visit from Week 2 to Week 10, collected predose, and at 0.5, 1, 2, 3, 4, and 6 hours after supervised dosing in the clinic.

Changes from baseline in inflammatory biomarkers including high-sensitivity C-reactive protein (hs-CRP), fecal calprotectin, and fecal lactoferrin were evaluated over time for the induction studies and the Maintenance Study.

Safety: Safety was evaluated by assessment of clinical laboratory tests, physical examinations, vital signs measurements, electrocardiograms (ECGs) at various time points during the study, and by the documentation of adverse events (AEs).

Statistical Methods:

Efficacy: The Full Analysis Set (FAS) was the primary analysis set used for the efficacy analyses.

Induction Studies (Cohort A Induction Study and Cohort B Induction Study)

For the induction studies, the FAS included all randomized subjects who took at least 1 dose of study drug. The primary efficacy endpoint in the induction studies were the proportion of subjects achieving EBS remission at Week 10. The primary analyses consisted of a superiority test of filgotinib 200 mg compared with placebo and filgotinib 100 mg compared with placebo based on the primary endpoint. For each induction study, a stratified Cochran-Mantel-Haenszel (CMH) test was used to compare the treatment effect between the filgotinib 200 mg group and placebo and between the filgotinib 100 mg group and placebo, separately. The CMH tests were stratified by concomitant use of oral, systemic corticosteroids at Day 1, and concomitant use of immunomodulators at Day 1 for the Cohort A Induction Study, and were stratified by concomitant use of oral, systemic corticosteroids at Day 1, concomitant use of immunomodulators at Day 1, and exposure to biologic agents (≤ 1, > 1) for the Cohort B Induction Study. A Bonferroni approach with equal alpha allocation of 0.025 (2-sided) to each filgotinib dose group comparison with placebo was used to control the overall study-wide type I error rate at 0.05 within each study. To protect the integrity of the induction studies due to the unblinded interim futility analysis for each induction study, an alpha of 0.00001 was spent for

each filgotinib dose group comparison to placebo. As a result, a p-value of less than 0.02499 (2-sided) was needed to declare statistical significance for the final primary analysis of each filgotinib dose group in the induction studies.

If the superiority of filgotinib 200 mg over placebo or filgotinib 100 mg over placebo was established in the primary analysis, then the next key secondary hypothesis in the same filgotinib dosing regimen was tested at the same alpha level in the following order:

- The MCS remission rate in the filgotinib group is equal to the MCS remission rate in the placebo group at Week 10
- The endoscopic subscore of 0 rate in the filgotinib group is equal to the endoscopic subscore of 0 rate in the placebo group at Week 10
- The Geboes histologic remission rate in the filgotinib group is equal to the Geboes histologic remission rate in the placebo group at Week 10
- The MCS remission (alternative definition) rate in the filgotinib group is equal to the MCS remission (alternative definition) rate in the placebo group at Week 10

Once all hypotheses within the same filgotinib dosing regimen were rejected, then the respective 0.02499 alpha could be passed on to the other dosing regimen's hypotheses, that is, all hypotheses in the other filgotinib dosing regimen would be tested at 0.04998 (2-sided) for the induction studies. If an endpoint within a filgotinib dosing regimen failed to reach statistical significance, then formal sequential testing was stopped and only nominal significance was reported for the remaining endpoints within that filgotinib dosing regimen. If not all primary and key secondary hypotheses within the same filgotinib dosing regimen could be rejected, all hypotheses in the other filgotinib dosing regimen were still tested at 0.02499 (2-sided).

Maintenance Study

The FAS for the Maintenance Study included all subjects from the filgotinib 200 mg or filgotinib 100 mg groups in the induction studies who achieved EBS remission or MCS response at Week 10, who were rerandomized and took at least 1 dose of study drug in the Maintenance Study. The primary efficacy endpoint in the Maintenance Study was the proportion of subjects achieving EBS remission at Week 58. For the Maintenance Study, a CMH test was used to compare the treatment effect between filgotinib 200 mg and placebo and between filgotinib 100 mg and placebo. The CMH test was stratified by participation in the Cohort A Induction Study or the Cohort B Induction Study, concomitant use of oral, systemic corticosteroids at maintenance baseline, and concomitant use of immunomodulators at maintenance baseline. Since there was no interim analysis for the Maintenance Study, the significance level for the final primary analysis was at the 0.025 (2-sided) level for each filgotinib dose group compared with placebo.

If the superiority of filgotinib 200 mg over placebo or filgotinib 100 mg over placebo was established in the primary analysis for the Maintenance Study, then the next key secondary hypothesis in the same filgotinib dosing regimen was tested at the same alpha level in the following order:

- The 6-month corticosteroid-free EBS remission rate in the filgotinib group is equal to the 6-month corticosteroid-free EBS remission rate in the placebo group at Week 58

- The sustained EBS remission rate in the filgotinib group is equal to the sustained EBS remission rate in the placebo group at Week 58
- The MCS remission rate in the filgotinib group is equal to the MCS remission rate in the placebo group at Week 58
- The endoscopic subscore of 0 rate in the filgotinib group is equal to the endoscopic subscore of 0 rate in the placebo group at Week 58
- The Geboes histologic remission rate in the filgotinib group is equal to the Geboes histologic remission rate in the placebo group at Week 58
- The MCS remission (alternative definition) rate in the filgotinib group is equal to the MCS remission (alternative definition) rate in the placebo group at Week 58

The same approach described for the induction studies was applied to the Maintenance Study at the alpha level of 0.025 (2-sided) for each filgotinib dose group compared with placebo.

Induction and Maintenance Studies

A similar stratified CMH test was used to compare the percentage difference between subjects in each filgotinib group and the placebo group for dichotomous key secondary and exploratory efficacy endpoints (MCS remission at Week 10/Week 58, endoscopic subscore of 0 at Week 10/Week 58, Geboes histologic remission at Week 10/Week 58, MCS remission [alternative definition] at Week 10/Week 58, 6-month corticosteroid-free EBS remission at Week 58, sustained EBS remission at Week 58, 6-month corticosteroid-free MCS remission at Week 58, sustained MCS remission at Week 58, novel histologic outcomes at Week 10/Week 58, endoscopic response at Week 10/Week 58, MCS response at Week 10/Week 58, and EBS remission [alternative definition] at Week 10/Week 58), subjects who did not have sufficient measurements to determine the endpoint were considered nonresponders (ie, nonresponder imputation [NRI]).

For MCS and partial MCS, descriptive statistics for the absolute values and change from baseline values were summarized, differences of mean change from induction baseline/maintenance baseline between each filgotinib dose group and placebo were tested using an analysis of covariance (ANCOVA) model adjusting for stratification factors and induction baseline or maintenance baseline value, respectively, with a last observation carried forward (LOCF) approach to impute missing values.

In addition to the FAS, the primary endpoints were also evaluated using the Per-Protocol (PP) Analysis Set. Additional analyses for the primary endpoint included sensitivity analyses based on locally read endoscopic subscore, analyses using different approaches for missing data imputation, and analyses excluding US/Korea non-dual refractory males who took placebo treatment for comparison between the filgotinib 200 mg and the placebo group in the Cohort B Induction Study.

Pharmacokinetics/Pharmacodynamics: Concentrations of filgotinib and GS-829845 in plasma were determined using validated bioanalytical assays. Steady-state PK parameters of filgotinib and GS-829845 were determined in subjects in the PK Substudy Analysis Set. The following plasma PK parameters were estimated for subjects participating in the substudy, as applicable: AUC_{last}, AUC_{tau}, C_{max}, T_{max}, C_{tau}, and CL_{ss}/F.

Biomarker analyses were conducted using the Biomarker Analysis Set. To evaluate treatment effect on biomarkers including serum hs-CRP, fecal calprotectin, and fecal lactoferrin, descriptive statistics including baseline, change from baseline and percent change from baseline at each postbaseline time point were provided.

Safety: All safety analyses were performed using the Safety Analysis Set. Adverse event data were summarized by treatment group using descriptive statistics. Clinical and laboratory AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 22.1.

Adverse events of interest (AEIs) were identified by the use of either Standardized MedDRA Queries (SMQs) or Gilead MedDRA Search Term (MST) lists. Adverse events of interest included all infections, serious infections, herpes zoster infections, opportunistic infections, malignancy excluding nonmelanoma skin cancers, nonmelanoma skin cancers, gastrointestinal perforations, and thromboembolic events (venous thrombosis, pulmonary embolism, arterial thrombosis, and cerebrovascular events).

Summaries of laboratory data were provided for the Safety Analysis Set. The analysis was based on values reported in conventional units.

SUMMARY OF RESULTS:

Subject Disposition and Demographics:

Cohort A Induction Study

A total of 1090 subjects were screened and 660 subjects were randomized to receive study drug in the Cohort A Induction Study (filgotinib 200 mg: 245 subjects; filgotinib 100 mg: 278 subjects; placebo: 137 subjects). Overall, 625 subjects (94.8%) completed study drug dosing through Week 10 (filgotinib 200 mg: 237 subjects, 96.7%; filgotinib 100 mg: 260 subjects, 93.9%; placebo: 128 subjects, 93.4%), and 618 subjects (93.8%) completed the Cohort A Induction Study.

The mean (SD) age of subjects was 42 (13.1) years. Fewer than half of subjects were female (44.3%) and most subjects were white (68.6%) or Asian (29.4%). Most subjects (90.0%) were from countries outside of the US. Demographics and other baseline characteristics were balanced across treatment groups.

The mean (SD) duration of UC from diagnosis to first dose of study drugs was 6.8 (7.20) years across all treatment groups. Mean (SD) MCS at baseline was 8.6 (1.36), and 52.4% of subjects had an MCS ≥ 9. In total, 55.8% of subjects had an endoscopic subscore of 3 at baseline. With respect to concomitant immunosuppressant use, the proportions of subjects taking only systemic corticosteroids or only immunomodulators at baseline were 23.5% and 22.6%, respectively. Overall, 7.1% of subjects were taking both systemic corticosteroids and immunomodulators, while 46.7% were taking neither systemic corticosteroids nor immunomodulators.

Cohort B Induction Study

A total of 950 subjects were screened and 691 subjects were randomized to receive study drug in the Cohort B Induction Study (filgotinib 200 mg: 262 subjects; filgotinib 100 mg: 286 subjects; placebo: 143 subjects). Overall, 635 subjects (92.2%) completed study drug dosing through Week 10 (filgotinib 200 mg: 242 subjects, 92.4%; filgotinib 100 mg: 265 subjects, 93.0%; placebo: 128 subjects, 90.1%), and 623 subjects (90.4%) completed the Cohort B Induction Study.

The mean (SD) age of subjects was 43 (14.4) years. Fewer than half of subjects were female (39.0%) and most subjects were white (72.6%) or Asian (18.6%). Most subjects (83.3%) were from countries outside of the US. Demographics and other baseline characteristics were balanced across treatment groups.

The mean (SD) duration of UC from diagnosis to first dose of study drugs was 9.8 (7.56) years across all treatment groups. Mean (SD) MCS at baseline was 9.3 (1.35), and 73.7% of subjects had an MCS $\geq$ 9. In total, 77.8% of subjects had an endoscopic subscore of 3 at baseline.

Prior use of a TNF-α antagonist was reported for 92.6% of subjects and prior use of vedolizumab was reported for 57.2% of subjects. Prior use of both a TNF-α antagonist and vedolizumab was reported for 50.9% of subjects. The use of at least 3 biologic agents was reported in 30.9% of subjects. With respect to concomitant immunosuppressant use, the proportions of subjects taking only systemic corticosteroids or only immunomodulators were 36.0% and 12.9%, respectively. Overall, 9.7% of subjects were taking both systemic corticosteroids and immunomodulators at baseline, while 41.4% of subjects were taking neither systemic corticosteroids nor immunomodulators.

Maintenance Study

Of the 1241 subjects who completed the induction studies, 664 subjects were rerandomized or continued on placebo in the Maintenance Study. A total of 150 subjects (74.3%) in the filgotinib 200 mg group completed study drug dosing through Week 58 compared with 41 subjects (41.4%) in the respective placebo group, and 104 subjects (58.1%) in the filgotinib 100 mg group completed study drug dosing through Week 58 compared with 42 subjects (46.2%) in the respective placebo group. A total of 64 subjects (68.8%) in the induction placebo to maintenance placebo group completed study drug dosing through Week 58.

The mean (SD) age of subjects was 43 (13.4) years. Approximately half of subjects were female (48.5%) and most subjects were white (70.8%) or Asian (26.1%). Most subjects (88.0%) were from countries outside of the US. Demographics and other baseline characteristics were generally balanced across treatment groups.

The mean (SD) duration of UC from diagnosis to baseline in the induction studies was 8.3 (7.64) years. Across treatment groups, 58.9% of subjects entered the Maintenance Study from the Cohort A Induction Study (biologic-naive subjects) and 41.1% entered the Maintenance Study from the Cohort B Induction Study (biologic-experienced subjects). Prior use of a TNF-α antagonist was reported for 37.3% of subjects and prior use of vedolizumab was reported for 20.5% of subjects. Prior use of both a TNF-α antagonist and vedolizumab was reported for 17.3% of subjects. The use of at least 3 biologic agents was reported in 12.3% of subjects.

With respect to concomitant immunosuppressant use, the proportions of subjects taking only systemic corticosteroids or only immunomodulators were 31.2% and 17.8%, respectively. Overall, 9.2% of subjects were taking both systemic corticosteroids and immunomodulators at baseline, while 41.9% of subjects were taking neither systemic corticosteroids nor immunomodulators.

Efficacy Results:

Cohort A Induction Study

Primary and Key Secondary Endpoints

Filgotinib 200 mg met the primary efficacy endpoint; a statistically significantly higher proportion of subjects achieved EBS remission at Week 10 in the filgotinib 200 mg group compared with the placebo group. Filgotinib 100 mg did not meet the primary endpoint.

Pairwise comparisons for each filgotinib dose with placebo were as follows:

- Filgotinib 200 mg: 26.1%, placebo: 15.3%; difference in proportions: 10.8%, 95% CI: 2.1% to 19.5%, p 0.0157
- Filgotinib 100 mg: 19.1%, placebo: 15.3%; difference in proportions: 3.8%, 95% CI: 4.3% to 12.0%, p 0.3379

Filgotinib 200 mg met all key secondary endpoints. Pairwise comparisons for each filgotinib dose with placebo were as follows:

MCS Remission

- Filgotinib 200 mg: 24.5%, placebo: 12.4%; difference in proportions: 12.1%, 95% CI: 3.8% to 20.4%, p 0.0053
- Filgotinib 100 mg: 17.0%, placebo: 12.4%; difference in proportions: 4.6%, 95% CI: 3.1% to 12.2%, p 0.2295

Endoscopic Subscore of 0

- Filgotinib 200 mg: 12.2%, placebo: 3.6%; difference in proportions: 8.6%, 95% CI: 2.9% to 14.3%, p 0.0047
- Filgotinib 100 mg: 5.8%, placebo: 3.6%; difference in proportions: 2.2%, 95% CI: 2.6% to 6.8%, p 0.3495

Geboes Histologic Remission

- Filgotinib 200 mg: 35.1%, placebo: 16.1%; difference in proportions: 19.0%, 95% CI: 9.9% to 28.2%, $p < 0.0001$
- Filgotinib 100 mg: 23.8%, placebo: 16.1%; difference in proportions: 7.8%, 95% CI: 0.7% to 16.2%, p 0.0672

MCS Remission (Alternative Definition)

- Filgotinib 200 mg: 12.2%, placebo: 4.4%; difference in proportions: 7.9%, 95% CI: 1.9% to 13.8%, p 0.0105
- Filgotinib 100 mg: 8.7%, placebo: 4.4%; difference in proportions: 4.3%, 95% CI: 1.0% to 9.6%, p 0.1062

Cohort B Induction Study

Primary and Key Secondary Endpoints

Filgotinib 200 mg met the primary efficacy endpoint; a statistically significantly higher proportion of subjects achieved EBS remission at Week 10 in the filgotinib 200 mg group

compared with the placebo group. Filgotinib 100 mg did not meet the primary endpoint. Pairwise comparisons for each filgotinib dose with placebo were as follows:

- Filgotinib 200 mg: 11.5%, placebo: 4.2%; difference in proportions: 7.2%, 95% CI: 1.6% to 12.8%, p 0.0103
- Filgotinib 100 mg: 9.5%, placebo: 4.2%; difference in proportions: 5.2%, 95% CI: 0.0% to 10.5%, p 0.0645

Filgotinib 200 mg did not meet any key secondary endpoints. Pairwise comparisons for each filgotinib dose with placebo were as follows:

MCS Remission

- Filgotinib 200 mg: 9.5%, placebo: 4.2%; difference in proportions: 5.3%, 95% CI: 0.1% to 10.7%, p 0.0393
- Filgotinib 100 mg: 6.0%, placebo: 4.2%; difference in proportions: 1.7%, 95% CI: 3.1% to 6.6%, p 0.5308

Endoscopic Subscore of 0

- Filgotinib 200 mg: 3.4%, placebo: 2.1%; difference in proportions: 1.3%, 95% CI: 2.5% to 5.1%, p 0.4269
- Filgotinib 100 mg: 2.1%, placebo: 2.1%; difference in proportions: 0.0%, 95% CI: 3.4% to 3.4%, p 0.9987

Geboes Histologic Remission

- Filgotinib 200 mg: 19.8%, placebo: 8.5%; difference in proportions: 11.4%, 95% CI: 4.2% to 18.6%, p 0.0019
- Filgotinib 100 mg: 13.7%, placebo: 8.5%; difference in proportions: 5.2%, 95% CI: 1.4% to 11.8%, p 0.1286

MCS Remission (Alternative Definition)

- Filgotinib 200 mg: 3.8%, placebo: 2.1%; difference in proportions: 1.7%, 95% CI: 2.2% to 5.6%, p 0.3084
- Filgotinib 100 mg: 2.1%, placebo: 2.1%; difference in proportions: 0.0%, 95% CI: 3.4% to 3.4%, p 0.9109

Maintenance Study

Primary and Key Secondary Endpoints

Both filgotinib 200 mg and filgotinib 100 mg met the primary efficacy endpoint; a statistically significantly higher proportion of subjects achieved EBS remission at Week 58 in the filgotinib 200 mg and filgotinib 100 mg groups compared with respective placebo groups. Pairwise comparisons for each filgotinib dose with respective placebo were as follows:

- Filgotinib 200 mg: 37.2%, respective placebo: 11.2%; difference in proportions: 26.0%, 95% CI: 16.0% to 35.9%, $p < 0.0001$
- Filgotinib 100 mg: 23.8%, respective placebo: 13.5%; difference in proportions: 10.4%, 95% CI: 0.0% to 20.7%, p 0.0420

Filgotinib 200 mg met all key secondary endpoints, and filgotinib 100 mg did not meet any key secondary endpoints. Pairwise comparisons for each filgotinib dose with respective placebo were as follows:

6-Month Corticosteroid-Free EBS Remission

- Filgotinib 200 mg: 27.2%, respective placebo: 6.4%; difference in proportions: 20.8%, 95% CI: 7.7% to 33.9%, p 0.0055
- Filgotinib 100 mg: 13.6%, respective placebo: 5.4%; difference in proportions: 8.2%, 95% CI: 4.2% to 20.6%, p 0.1265

Sustained EBS Remission

- Filgotinib 200 mg: 18.1%, respective placebo: 5.1%; difference in proportions: 13.0%, 95% CI: 5.3% to 20.6%, p 0.0024
- Filgotinib 100 mg: 8.7%, respective placebo: 7.9%; difference in proportions: 0.9%, 95% CI: 7.0% to 8.7%, p 0.7951

MCS Remission

- Filgotinib 200 mg: 34.7%, respective placebo: 9.2%; difference in proportions: 25.5%, 95% CI: 16.0% to 35.0%, $p < 0.0001$
- Filgotinib 100 mg: 22.7%, respective placebo: 13.5%; difference in proportions: 9.2%, 95% CI: 1.1% to 19.5%, p 0.0658

Endoscopic Subscore of 0

- Filgotinib 200 mg: 15.6%, respective placebo: 6.1%; difference in proportions: 9.5%, 95% CI: 1.8% to 17.1%, p 0.0157
- Filgotinib 100 mg: 13.4%, respective placebo: 7.9%; difference in proportions: 5.5%, 95% CI: 2.9% to 13.9%, p 0.1808

Geboes Histologic Remission

- Filgotinib 200 mg: 38.2%, respective placebo: 13.3%; difference in proportions: 24.9%, 95% CI: 14.6% to 35.2%, $p < 0.0001$
- Filgotinib 100 mg: 27.9%, respective placebo: 18.0%; difference in proportions: 9.9%, 95% CI: 1.3% to 21.2%, p 0.0521

MCS Remission (Alternative Definition)

- Filgotinib 200 mg: 22.1%, respective placebo: 6.1%; difference in proportions: 16.0%, 95% CI: 7.8% to 24.2%, p 0.0005
- Filgotinib 100 mg: 12.2%, respective placebo: 7.9%; difference in proportions: 4.3%, 95% CI: 3.9% to 12.6%, p 0.2946

Sensitivity analyses results using Per-Protocol analysis, locally read endoscopic subscore analysis, and missing data imputation analyses were consistent with the primary efficacy endpoint analysis results for filgotinib 200 mg compared with placebo.

The treatment effect of filgotinib 200 mg compared with placebo in establishing EBS remission at Week 58 was consistent across all subgroups by stratification and demographic factors, disease characteristics, and prior biologic history.

Pharmacokinetics/Pharmacodynamics Results:

In the Cohort A Induction Study and the Cohort B Induction Study, the overall plasma concentration-time profile was similar between the filgotinib 200-mg dose and the filgotinib 100-mg dose, with higher filgotinib exposures at the 200-mg dose. Similar PK were observed between biologic-naive subjects and biologic-experienced subjects for both filgotinib and GS-829845.

In the Cohort A Induction Study and the Cohort B Induction Study, subjects in the filgotinib 200 mg and filgotinib 100 mg treatment groups had greater decreases in hs-CRP, fecal calprotectin, and fecal lactoferrin values at Week 10 compared with subjects inn the placebo group. Values of hs-CRP, fecal calprotectin, and fecal lactoferrin were generally unchanged for subjects who continued on filgotinib 200 mg or filgotinib 100 mg during the Maintenance Study.

Safety Results:

Cohort A Induction Study

Exposure

Overall, the mean (SD) durations of exposure to study drug were as follows:

- Filgotinib 200 mg: 11.0 (1.05) weeks
- Filgotinib 100 mg: 10.8 (2.03) weeks
- Placebo: 10.8 (1.56) weeks

Death, Serious Adverse Events, Discontinuations Due to Adverse Events, Common Adverse Events, and Adverse Events by Severity

Death

No deaths were reported during the Cohort A Induction Study.

Serious Adverse Events

Serious adverse events (SAEs) were reported by treatment group as follows: filgotinib 200 mg: 3 subjects (1.2%), filgotinib 100 mg: 13 subjects (4.7%), and placebo: 4 subjects (2.9%). The most commonly occurring SAE was colitis ulcerative.

Discontinuations Due to Adverse Events

Adverse events that led to premature discontinuation of study drug by treatment group were as follows: filgotinib 200 mg: 5 subjects (2.0%), filgotinib 100 mg: 6 subjects (2.2%), and placebo: 4 subjects (2.9%). The most commonly occurring AE leading to discontinuation of study drug was colitis ulcerative.

Common Adverse Events

The most commonly reported system organ classes (SOCs) by treatment group were:

- Gastrointestinal disorders:

  Filgotinib 200 mg: 37 subjects (15.1%)

  Filgotinib 100 mg: 35 subjects (12.6%)

  Placebo: 24 subjects (17.5%)

- Infections and infestations:

  Filgotinib 200 mg: 27 subjects (11.0%)

  Filgotinib 100 mg: 27 subjects (9.7%)

  Placebo: 8 subjects (5.8%)

Within the gastrointestinal disorders SOC, the most commonly reported high-level terms (HLTs) were:

- Colitis (excl infective):

  Filgotinib 200 mg: 6 subjects (2.4%)

  Filgotinib 100 mg: 6 subjects (2.2%)

  Placebo: 8 subjects (5.8%)

- Nausea and vomiting symptoms:

  Filgotinib 200 mg: 12 subjects (4.9%)

  Filgotinib 100 mg: 6 subjects (2.2%)

  Placebo: 5 subjects (3.6%)

Within the infections and infestations SOC, the most commonly reported HLT was upper respiratory tract infections:

- Filgotinib 200 mg: 13 subjects (5.3%)
- Filgotinib 100 mg: 13 subjects (4.7%)
- Placebo: 3 subjects (2.2%)

The most commonly reported AEs by treatment group were as follows:

- Filgotinib 200 mg: headache (11 subjects, 4.5%), nausea (8 subjects, 3.3%), and nasopharyngitis (7 subjects, 2.9%)
- Filgotinib 100 mg: headache (12 subjects, 4.3%), anemia (11 subjects, 4.0%), and nasopharyngitis (9 subjects, 3.2%)
- Placebo: colitis ulcerative (7 subjects, 5.1%), headache (6 subjects, 4.4%), and anemia (5 subjects, 3.6%)

Adverse Events by Severity

Throughout the study, most of the AEs reported across all treatment groups were Grade 1 or 2 in severity. Overall, the proportion of subjects with Grade 3 or higher AEs, by treatment group, were as follows: filgotinib 200 mg: 5 subjects (2.0%), filgotinib 100 mg: 22 subjects (7.9%), and placebo: 11 subjects (8.0%).

Adverse Events of Interest

Infections were reported as follows: filgotinib 200 mg: 27 subjects (11.0%), filgotinib 100 mg: 27 subjects (9.7%), and placebo: 8 subjects (5.8%). Overall, the most commonly reported infection across all treatment groups was nasopharyngitis. Serious infections were reported as follows: filgotinib 200 mg: 1 subject (0.4%), filgotinib 100 mg: 2 subjects (0.7%), and placebo: 1 subject (0.7%). Two subjects (0.8%) who received filgotinib 200 mg reported herpes zoster infections; Grade 1 in 1 subject and Grade 2 in 1 subject. Esophageal candidiasis (Grade 1) was reported for 1 subject (0.4%) who received filgotinib 200 mg. Colon cancer (Grade 2) was reported for 1 subject (0.4%) who received filgotinib 100 mg. Basal cell carcinoma (Grade 1) was reported for 1 subject (0.7%) who received placebo. Procedural intestinal perforation (Grade 3) was reported in 1 subject (0.7%) who received placebo. No thromboembolic events (venous thrombosis, pulmonary embolism, arterial thrombosis, or cerebrovascular events) were reported.

Clinical Laboratory Evaluations

Median values for hemoglobin, lymphocyte, platelet, monocyte, basophil, and eosinophil count were similar across the treatment groups and stable over the course of treatment. Median white blood cell (WBC) counts were slightly decreased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: $0.59 \times 10^3/\mu L$ and $0.39 \times 10^3/\mu L$, respectively) compared with placebo (median change from baseline at Week 10: $0.06 \times 10^3/\mu L$). Median neutrophil counts were slightly decreased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: $0.52 \times 10^3/\mu L$ and $0.26 \times 10^3/\mu L$, respectively) compared with placebo (median change from baseline at Week 10: $0.12 \times 10^3/\mu L$).

Median values for most clinical chemistry parameters including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, total bilirubin, serum creatinine, CL_{cr}, fasting triglycerides, and fasting low-density lipoprotein (LDL) to high-density lipoprotein (HDL) ratio were similar across the treatment groups and stable over the course of treatment. Median creatine kinase (CK) values slightly increased over time in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 37 U/L and 27 U/L, respectively) compared with placebo (median change from baseline at Week 10: 4 U/L). Median fasting total cholesterol values slightly increased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 19 mg/dL and 15 mg/dL, respectively) compared with a slight increase for placebo (median change from baseline at Week 10: 6 mg/dL). Median fasting LDL values slightly increased across the treatment groups (median changes from baseline at Week 10 were as follows for filgotinib 200 mg: 10 mg/dL, filgotinib 100 mg: 7 mg/dL, and placebo: 6 mg/dL). Median fasting HDL values slightly increased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 14 mg/dL and 9 mg/dL, respectively) compared with placebo (median change from baseline at Week 10: 3 mg/dL).

Graded Laboratory Abnormalities

Grade 3 or 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 25 subjects (10.2%), filgotinib 100 mg: 20 subjects (7.4%), and placebo: 8 subjects (5.8%). Grade 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 3 subjects (1.2%), filgotinib 100 mg: 3 subjects (1.1%), and placebo: 1 subject (0.7%).

The most commonly reported Grade 3 or 4 laboratory abnormalities for chemistry evaluations were hypophosphatemia and CK.

Grade 3 hypophosphatemia laboratory abnormalities were reported in 6 subjects (filgotinib 200 mg: 3 subjects, 1.2% and filgotinib 100 mg: 3 subjects, 1.1%). Grade 4 hypophosphatemia laboratory abnormalities were reported in 2 subjects (filgotinib 200 mg: 1 subject, 0.4% and filgotinib 100 mg: 1 subject, 0.4%).

Grade 3 CK increased laboratory abnormalities were reported in 2 subjects (filgotinib 200 mg: 1 subject, 0.4% and filgotinib 100 mg: 1 subject, 0.4%). Grade 4 CK increased laboratory abnormalities were reported in 3 subjects (filgotinib 200 mg: 2 subjects, 0.8% and filgotinib 100 mg: 1 subject, 0.4%). No rhabdomyolysis was reported.

Complete Blood Count-Related Laboratory Evaluations

The incidences of hemoglobin decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 5 subjects (2.0%)
- Filgotinib 100 mg: 7 subjects (2.6%)
- Placebo: 2 subjects (1.5%)

The incidences of WBC count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 2 subjects (0.8%)
- Filgotinib 100 mg: 1 subject (0.4%)
- Placebo: 1 subject (0.7%)

The incidences of neutrophil count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 2 subjects (0.8%)
- Filgotinib 100 mg: 2 subjects (0.7%)

  1 subject (0.4%) experienced a worst postbaseline Grade 4 neutrophil count decrease
- Placebo: 2 subjects (1.5%)

The incidences of lymphocyte count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 7 subjects (2.9%)
- Filgotinib 100 mg: 2 subjects (0.7%)
- Placebo: 3 subjects (2.2%)

No subjects experienced worsening in Common Terminology Criteria for Adverse Events (CTCAE) grade from < Grade 3 at baseline to ≥ Grade 3 at postbaseline for platelet count decrease.

Liver-Related Laboratory Evaluations

No subjects had ALT > 5 × upper limit of normal (ULN). One subject (0.4%) in the filgotinib 100 mg treatment group had AST > 5 × ULN.

ALT > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 2 subjects (0.8%)
- Filgotinib 100 mg: 2 subjects (0.7%)
- Placebo: 1 subject (0.7%)

AST > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 0 subjects
- Filgotinib 100 mg: 2 subjects (0.7%)
- Placebo: 1 subject (0.7%)

Throughout the study, no subject had ALT or AST > 3 × ULN, and total bilirubin > 2 × ULN at the same postbaseline visit date.

Vital Signs, Physical Findings, and Other Observations Related to Safety

There were no marked changes from baseline in vital signs parameters, body weight, or body mass index (BMI). One subject (0.4%) in the filgotinib 200 mg group had a clinically significant shift in ECG parameters from normal at baseline to clinically significant abnormal at Week 10.

Cohort B Induction Study

Exposure

Overall, the mean (SD) durations of exposure to study drug were as follows:

- Filgotinib 200 mg: 10.6 (1.93) weeks
- Filgotinib 100 mg: 10.7 (1.80) weeks
- Placebo: 10.5 (2.22) weeks

Death, Serious Adverse Events, Discontinuations Due to Adverse Events, Common Adverse Events, and Adverse Events by Severity

Death

No deaths were reported during the Cohort B Induction Study.

Serious Adverse Events

Serious adverse events were reported by treatment group as follows: filgotinib 200 mg: 19 subjects (7.3%), filgotinib 100 mg: 15 subjects (5.3%), and placebo: 9 subjects (6.3%). The most commonly occurring SAE was colitis ulcerative.

Discontinuations Due to Adverse Events

Adverse events that led to premature discontinuation of study drug by treatment group were as follows: filgotinib 200 mg: 18 subjects (6.9%), filgotinib 100 mg: 14 subjects (4.9%), and placebo: 10 subjects (7.0%). The most commonly occurring AE leading to discontinuation of study drug was colitis ulcerative.

Common Adverse Events

The most commonly reported SOCs by treatment group were:

- Gastrointestinal disorders:

  Filgotinib 200 mg: 67 subjects (25.6%)

  Filgotinib 100 mg: 57 subjects (20.0%)

  Placebo: 29 subjects (20.4%)

- Infections and infestations:

  Filgotinib 200 mg: 65 subjects (24.8%)

  Filgotinib 100 mg: 55 subjects (19.3%)

  Placebo: 31 subjects (21.8%)

Within the gastrointestinal disorders SOC, the most commonly reported HLTs were:

- Colitis (excl infective):

  Filgotinib 200 mg: 21 subjects (8.0%)

  Filgotinib 100 mg: 16 subjects (5.6%)

  Placebo: 12 subjects (8.5%)

- Nausea and vomiting symptoms:

  Filgotinib 200 mg: 11 subjects (4.2%)

  Filgotinib 100 mg: 17 subjects (6.0%)

  Placebo: 8 subjects (5.6%)

Within the infections and infestations SOC, the most commonly reported HLT was upper respiratory tract infections:

- Filgotinib 200 mg: 36 subjects (13.7%)
- Filgotinib 100 mg: 31 subjects (10.9%)
- Placebo: 19 subjects (13.4%)

The most commonly reported AEs by treatment group were as follows:

- Filgotinib 200 mg: colitis ulcerative (21 subjects, 8.0%), nasopharyngitis (20 subjects, 7.6%), and headache (19 subjects, 7.3%)
- Filgotinib 100 mg: nasopharyngitis (20 subjects, 7.0%), nausea (16 subjects, 5.6%), and colitis ulcerative (15 subjects, 5.3%)
- Placebo: colitis ulcerative (11 subjects, 7.7%), nasopharyngitis (11 subjects, 7.7%), anemia (10 subjects, 7.0%), abdominal pain (9 subjects, 6.3%), and headache (9 subjects, 6.3%)

Adverse Events by Severity

Throughout the study, most of the AEs reported across all treatment groups were Grade 1 or 2 in severity. Overall, the proportion of subjects with Grade 3 or higher AEs, by treatment group, were as follows: filgotinib 200 mg: 30 subjects (11.5%), filgotinib 100 mg: 26 subjects (9.1%), and placebo: 20 subjects (14.1%).

Adverse Events of Interest

Infections were reported as follows: filgotinib 200 mg: 65 subjects (24.8%), filgotinib 100 mg: 55 subjects (19.3%), and placebo: 31 subjects (21.8%). Overall, the most commonly reported infection across all treatment groups were nasopharyngitis and upper respiratory tract infection. Serious infections were reported as follows: filgotinib 200 mg: 2 subjects (0.8%), filgotinib 100 mg: 4 subjects (1.4%), and placebo: 2 subjects (1.4%). Herpes zoster infections were reported for 1 subject who received filgotinib 200 mg (0.4%; Grade 2) and 1 subject who received filgotinib 100 mg (0.4%; Grade 1). No opportunistic infections were reported. Breast cancer (Grade 2) was reported for 1 subject (0.4%) who received filgotinib 200 mg. Nonmelanoma skin cancer was reported for 2 subjects (0.8%) who received filgotinib 200 mg (Grade 1 basal cell carcinoma in 1 subject and Grade 1 Bowen's disease in 1 subject). No gastrointestinal perforations were reported. One subject (0.4%) who received filgotinib 200 mg experienced a pulmonary embolism (Grade 3). Cerebrovascular accident (Grade 4) was reported in 1 subject (0.7%) who received placebo. No venous thrombosis or arterial thrombosis events were reported.

Clinical Laboratory Evaluations

Median values for hemoglobin, lymphocyte, platelet, monocyte, basophil, and eosinophil count were similar across the treatment groups and stable over the course of treatment. Median WBC counts slightly decreased in all treatment groups (median change from baseline at Week 10 for filgotinib 200 mg: $0.93 \times 10^3/\mu L$; filgotinib 100 mg: $0.57 \times 10^3/\mu L$; and placebo: $0.51 \times 10^3/\mu L$). Median neutrophil counts slightly decreased in all treatment groups (median change from baseline at Week 10 was as follows for filgotinib 200 mg: $0.62 \times 10^3/\mu L$, filgotinib 100 mg $0.34 \times 10^3/\mu L$, and placebo: $0.46 \times 10^3/\mu L$).

Median values for most clinical chemistry parameters including ALT, AST, alkaline phosphatase, total bilirubin, serum creatinine, CL_{cr}, fasting triglycerides, and fasting LDL to HDL ratio were similar across the treatment groups and stable over the course of treatment. Median CK values slightly increased over time in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 39 U/L and 24 U/L, respectively) compared with placebo (median change from baseline at Week 10: 3 U/L). Median fasting total cholesterol values slightly increased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 20 mg/dL and 12 mg/dL, respectively) compared with placebo (median change from baseline at Week 10: 0 mg/dL). Median fasting LDL values slightly increased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 12 mg/dL and 9 mg/dL, respectively) compared with placebo (median change from baseline at Week 10: 2 mg/dL). Median fasting HDL values slightly increased in the filgotinib 200 mg and 100 mg treatment groups (median change from baseline at Week 10: 15 mg/dL and 7 mg/dL, respectively) compared with placebo (median change from baseline at Week 10: 1 mg/dL).

Graded Laboratory Abnormalities

Grade 3 or 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 29 subjects (11.1%), filgotinib 100 mg: 36 subjects (12.6%), placebo: 16 subjects (11.3%). Grade 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 3 subjects (1.1%), filgotinib 100 mg: 1 subject (0.4%), and placebo: 1 subject (0.7%).

Grade 3 hypophosphatemia laboratory abnormalities were reported in 34 subjects (filgotinib 200 mg: 14 subjects, 5.4%, filgotinib 100 mg: 14 subjects, 4.9%, and placebo: 6 subjects, 4.2%). One subject (0.4%) in the filgotinib 100 mg group had a Grade 4 hypophosphatemia laboratory abnormality.

Grade 3 CK increased laboratory abnormalities were reported in 3 subjects (filgotinib 200 mg: 1 subject, 0.4% and filgotinib 100 mg: 2 subjects, 0.7%). Grade 4 CK increased laboratory abnormalities were reported in 3 subjects (1.1%) in the filgotinib 200 mg treatment group. No rhabdomyolysis was reported.

Complete Blood Count-Related Laboratory Evaluations

The incidences of hemoglobin decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 5 subjects (1.9%)
- Filgotinib 100 mg: 3 subjects (1.1%)
- Placebo: 6 subjects (4.2%)

The incidences of WBC count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 1 subject (0.4%)
- Filgotinib 100 mg: 0 subjects
- Placebo: 0 subjects

The incidences of neutrophil count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 1 subject (0.4%)
- Filgotinib 100 mg: 5 subjects (1.8%)
- Placebo: 0 subjects

The incidences of lymphocyte count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 4 subjects (1.5%)
- Filgotinib 100 mg: 8 subjects (2.8%)
- Placebo: 3 subjects (2.1%)

No subjects experienced worsening in CTCAE grade from < Grade 3 at baseline to ≥ Grade 3 at postbaseline for platelet count decrease.

Liver-Related Laboratory Evaluations

One subject (0.4%) in the filgotinib 200 mg treatment group had ALT > 10 × ULN and 2 subjects (1.4%) in the placebo group had ALT > 5 × ULN. One subject (0.4%) in the filgotinib 200 mg treatment group had AST > 5 × ULN.

ALT > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 1 subject (0.4%)
- Filgotinib 100 mg: 1 subject (0.4%)
- Placebo: 2 subjects (1.4%)

AST > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 4 subjects (1.5%)
- Filgotinib 100 mg: 0 subjects
- Placebo: 2 subjects (1.4%)

Throughout the study, no subject had ALT or AST > 3 × ULN, and total bilirubin > 2 × ULN at the same postbaseline visit date.

Vital Signs, Physical Findings, and Other Observations Related to Safety

There were no marked changes from baseline in vital signs parameters, body weight, or BMI. Two subjects (0.8%) in the filgotinib 200 mg treatment group had clinically significant shifts in ECG parameters from not clinically significant abnormal at baseline to clinically significant abnormal at Week 10.

Maintenance Study

Exposure

Overall, the mean (SD) durations of exposure to study drug were as follows:

- Filgotinib 200 mg: 39.4 (14.33) weeks

  Respective placebo: 28.8 (17.68) weeks
- Filgotinib 100 mg: 34.5 (16.84) weeks

  Respective placebo: 29.2 (18.57) weeks

Death, Serious Adverse Events, Discontinuations Due to Adverse Events, Common Adverse Events, and Adverse Events by Severity

Death

Deaths were reported for 2 subjects (1.0%) in the filgotinib 200 mg treatment group.

Serious Adverse Events

Serious adverse events were reported by treatment group as follows: filgotinib 200 mg: 9 subjects (4.5%), respective placebo: 0 subjects; and filgotinib 100 mg: 8 subjects (4.5%), respective placebo: 7 subjects (7.7%).

Discontinuations Due to Adverse Events

The incidences of AEs leading to premature discontinuation of study drug by treatment groups were as follows for filgotinib 200 mg: 7 subjects, 3.5%; respective placebo: 2 subjects, 2.0%; filgotinib 100 mg: 10 subjects, 5.6%; and respective placebo: 4 subjects, 4.4%. The most commonly occurring AE leading to discontinuation of study drug was colitis ulcerative.

Common Adverse Events

The most commonly reported SOCs by treatment group were:

- Gastrointestinal disorders:

  Filgotinib 200 mg: 58 subjects (28.7%)

  - Respective placebo: 33 subjects (33.3%)

  Filgotinib 100 mg: 49 subjects (27.4%)

  - Respective placebo: 31 subjects (34.1%)

- Infections and infestations:

  Filgotinib 200 mg: 71 subjects (35.1%)

  - Respective placebo: 25 subjects (25.3%)

  Filgotinib 100 mg: 46 subjects (25.7%)

  - Respective placebo: 27 subjects (29.7%)

Within the gastrointestinal disorders SOC, the most commonly reported HLTs were:

- Colitis (excl infective):

  Filgotinib 200 mg: 23 subjects (11.4%)

  - Respective placebo: 20 subjects (20.2%)

  Filgotinib 100 mg: 20 subjects (11.2%)

  - Respective placebo: 16 subjects (17.6%)

- Gastrointestinal and abdominal pains (excl oral and throat):

  Filgotinib 200 mg: 11 subjects (5.4%)

  - Respective placebo: 6 subjects (6.1%)

  Filgotinib 100 mg: 10 subjects (5.6%)

  - Respective placebo: 3 subjects (3.3%)

Within the infections and infestations SOC, the most commonly reported HLT was upper respiratory tract infections:

- Filgotinib 200 mg: 43 subjects (21.3%)

  Respective placebo: 11 subjects (11.1%)

- Filgotinib 100 mg: 25 subjects (14.0%)

  Respective placebo: 10 subjects (11.0%)

The most commonly reported AEs by treatment group were as follows:

- Filgotinib 200 mg: nasopharyngitis (22 subjects, 10.9%), colitis ulcerative (21 subjects, 10.4%), and upper respiratory tract infection (11 subjects, 5.4%)

  Respective placebo: colitis ulcerative (20 subjects, 20.2%), arthralgia (7 subjects, 7.1%), abdominal pain (6 subjects, 6.1%), and nasopharyngitis (6 subjects, 6.1%)

- Filgotinib 100 mg: colitis ulcerative (19 subjects, 10.6%), nasopharyngitis (12 subjects, 6.7%), and headache (11 subjects, 6.1%)

  Respective placebo: colitis ulcerative (16 subjects, 17.6%), nasopharyngitis (6 subjects, 6.6%), and headache (5 subjects, 5.5%)

Adverse Events by Severity

Throughout the study, most of the AEs reported across all treatment groups were Grade 1 or 2 in severity. Overall, the proportion of subjects with Grade 3 or higher AEs, by treatment group, were as follows: filgotinib 200 mg: 16 subjects (7.9%), respective placebo: 7 subjects (7.1%); and filgotinib 100 mg: 11 subjects (6.1%), respective placebo: 10 subjects (11.0%).

Adverse Events of Interest

Infections were reported as follows: filgotinib 200 mg: 71 subjects (35.1%) and respective placebo: 25 subjects (25.3%); and filgotinib 100 mg: 46 subjects (25.7%) and respective placebo: 27 subjects (29.7%). Overall, the most commonly reported infection across all treatment groups was nasopharyngitis. Serious infections were reported as follows: filgotinib 200 mg: 2 subjects (1.0%) and respective placebo: 0 subjects; and filgotinib 100 mg: 3 subjects (1.7%) and respective placebo: 2 subjects (2.2%). Grade 2 herpes zoster infections were reported in 1 subject (0.5%) who received filgotinib 200 mg and 1 subject (1.1%) who received placebo (following induction filgotinib 100 mg). No opportunistic infections were reported. Malignant melanoma (Grade 3) was reported for 1 subject (0.5%) who received filgotinib 200 mg and colon cancer (Grade 3) was reported for 1 subject (0.6%) who received filgotinib 100 mg. Basal cell carcinoma (Grade 2) was reported in 1 subject (0.6%) who received filgotinib 100 mg. No gastrointestinal perforations were reported. Venous thrombosis events were reported in 2 subjects (2.2%) who received placebo. No pulmonary embolism was reported. Grade 2 transient ischemic attack was reported as both an arterial thrombosis event and a cerebrovascular event in 1 subject (0.6%) in the filgotinib 100 mg treatment group.

Clinical Laboratory Evaluations

Median values for hemoglobin, WBC, neutrophil, lymphocyte, platelet, monocyte, basophil, and eosinophil count were similar across the treatment groups and stable over the course of treatment.

Median values for most clinical chemistry parameters including ALT, AST, alkaline phosphatase, total bilirubin, serum creatinine, CL_{cr}, fasting total cholesterol, fasting HDL, fasting triglycerides, and fasting LDL to HDL ratio were similar across the treatment groups and stable over the course of treatment. Median CK values slightly increased over time in the filgotinib 200 mg and 100 mg treatment groups (median change from maintenance baseline at maintenance Week 47: 11 U/L and 9 U/L, respectively) compared with respective placebo groups (median change from maintenance baseline at maintenance Week 47: 30 U/L and 7 U/L, respectively).

Median fasting LDL values slightly increased in the filgotinib 200 mg treatment group compared with respective placebo (median change from maintenance baseline at maintenance Week 47: 7 mg/dL and 5 mg/dL, respectively) and were stable over the duration of treatment in the filgotinib100 mg treatment group and respective placebo (median change from maintenance baseline at maintenance Week 47: 4 mg/dL and 1 mg/dL, respectively).

Graded Laboratory Abnormalities

Grade 3 or 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 28 subjects (13.9%) and respective placebo: 13 subjects (13.4%); and filgotinib 100 mg: 22 subjects (12.6%) and respective placebo: 11 subjects (12.4%). The incidences of Grade 4 laboratory abnormalities were reported as follows: filgotinib 200 mg: 4 subjects (2.0%) and respective placebo: 1 subject (1.0%); and filgotinib 100 mg: 1 subject (0.6%), and respective placebo: 3 subjects (3.4%).

The most commonly reported Grade 3 or 4 laboratory abnormalities for chemistry evaluations were hypophosphatemia and CK.

Grade 3 hypophosphatemia laboratory abnormalities were reported in 16 subjects (filgotinib 200 mg: 5 subjects, 2.5%; respective placebo: 3 subjects, 3.1%; filgotinib 100 mg: 6 subjects, 3.4%; and respective placebo: 2 subjects, 2.2%). One subject (1.1%) in the placebo (following induction filgotinib 100 mg) group had a Grade 4 hypophosphatemia laboratory abnormality.

Grade 3 CK increased laboratory abnormalities were reported in 8 subjects (filgotinib 200 mg: 5 subjects, 2.5%; respective placebo: 1 subject, 1.0%; filgotinib 100 mg: 1 subject, 0.6%; and respective placebo: 1 subject, 1.1%). Grade 4 CK increased laboratory abnormalities were reported in 5 subjects (filgotinib 200 mg: 3 subjects, 1.5%; respective placebo: 1 subject, 1.0%; filgotinib 100 mg: 1 subject, 0.6%; and respective placebo: 0 subjects). No rhabdomyolysis was reported among any of these subjects.

Complete Blood Count-Related Laboratory Evaluations

The incidences of hemoglobin decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 3 subjects (1.5%)

  Respective placebo: 1 subject (1.0%)
- Filgotinib 100 mg: 1 subject (0.6%)

  Respective placebo: 1 subject (1.1%)

The incidences of WBC count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 1 subject (0.5%)

  Respective placebo: 0 subjects
- Filgotinib 100 mg: 0 subjects

  Respective placebo: 1 subject (1.1%)

The incidences of neutrophil count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 0 subjects

  Respective placebo: 2 subjects (2.1%)
- Filgotinib 100 mg: 3 subjects (1.7%)

  Respective placebo: 2 subjects (2.2%)
  - 1 subject (1.1%) experienced a worst postbaseline Grade 4 neutrophil count decrease

The incidences of lymphocyte count decrease < Grade 3 at baseline and ≥ Grade 3 postbaseline, by treatment group, were:

- Filgotinib 200 mg: 5 subjects (2.5%)

  Respective placebo: 1 subject (1.0%)
- Filgotinib 100 mg: 3 subjects (1.7%)

  Respective placebo: 1 subject (1.1%)

No subjects experienced worsening in CTCAE grade from < Grade 3 at baseline to ≥ Grade 3 at postbaseline for platelet count decrease.

Liver-Related Laboratory Evaluations

ALT > 10 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 1 subject (0.5%)

  No events were reported in the respective placebo group
- No events were reported in the filgotinib 100 mg group

  Respective placebo: 1 subject (1.1%).

AST > 10 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 1 subject (0.5%)

  No events were reported in the respective placebo group
- Filgotinib 100 mg: 1 subject (0.6%)

  Respective placebo: 1 subject (1.1%).

ALT > 5 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 1 subject (0.5%)

  No events were reported in the respective placebo group
- Filgotinib 100 mg: 3 subjects (1.7%)

  Respective placebo: 2 subjects (2.2%).

AST > 5 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 1 subject (0.5%)

  Respective placebo: 1 subject (1.0%)
- Filgotinib 100 mg: 1 subject (0.6%)

  Respective placebo: 2 subjects (2.2%).

ALT > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 4 subjects (2.0%)

  Respective placebo: 2 subjects (2.1%)

- Filgotinib 100 mg: 5 subjects (2.9%)

  Respective placebo: 2 subjects (2.2%)

AST > 3 × ULN abnormalities were reported by treatment group as follows:

- Filgotinib 200 mg: 2 subjects (1.0%)

  Respective placebo: 2 subjects (2.1%)

- Filgotinib 100 mg: 3 subjects (1.7%)

  Respective placebo: 2 subjects (2.2%)

Throughout the study, no subject had ALT or AST > 3 × ULN, and total bilirubin > 2 × ULN at the same postbaseline visit date.

Vital Signs, Physical Findings, and Other Observations Related to Safety

There were no marked changes from maintenance baseline in vital signs parameters, body weight, or BMI. One subject (0.8%) in the filgotinib 100 mg group with not clinically significant abnormal ECG at maintenance baseline had a clinically significant abnormal ECG at Week 15 of the Maintenance Study.

CONCLUSIONS:

The conclusions from Study GS-US-418-3898 are as follows:

Among biologic-naive subjects with moderately to severely active UC

- Treatment for 10 weeks with filgotinib 200 mg resulted in a significantly higher proportion of patients achieving EBS remission, MCS remission, an endoscopic subscore of 0, Geboes histologic remission, and MCS remission (alternative definition) compared with placebo.

Among biologic-experienced subjects with moderately to severely active UC

- Treatment for 10 weeks with filgotinib 200 mg resulted in a significantly higher proportion of patients achieving EBS remission, compared with placebo.

Among biologic-naive and biologic-experienced subjects with moderately to severely active UC who achieved a clinical response to induction treatment with filgotinib

- Treatment with filgotinib 200 mg for 47 weeks resulted in a significantly higher proportion of patients achieving EBS remission, 6-month corticosteroid-free EBS remission, sustained EBS remission, MCS remission, an endoscopic subscore of 0, Geboes histologic remission, and MCS remission (alternative definition) at Week 58 compared with placebo.
- Treatment with filgotinib 100 mg for 47 weeks resulted in a significantly higher proportion of patients achieving EBS remission compared with placebo.

Among biologic-naive and biologic-experienced subjects with moderately to severely active UC

- Filgotinib 100 mg and 200 mg were generally well tolerated, as evidenced by low rates of study treatment discontinuation due to AEs, SAEs, Grade 3 or higher AEs, serious infections, herpes zoster infections, opportunistic infections, gastrointestinal perforations, malignancies excluding nonmelanoma skin cancers, nonmelanoma skin cancers, thromboembolic events, and laboratory abnormalities.