Description of the Tranquillo phase 3 clinical program to assess ritlecitinib treatment in adults and adolescents with nonsegmental vitiligo

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BACKGROUND

- Vitiligo is an autoimmune skin disease characterized by pigment loss due to the destruction of melanocytes; vitiligo can often affect a patient's psychosocial health[1-7]
- No targeted systemic treatments are currently approved for nonsegmental vitiligo (NSV)[8]
- Ritlecitinib is an oral, selective inhibitor of JAK3 and the TEC family kinases that is under investigation for the treatment of NSV[9]
  - In a phase 2b study (NCT03715829), ritlecitinib 50 mg (±100- or 200-mg loading dose) once daily (QD) was effective and well tolerated in adults with active NSV over 48 weeks[9]

OBJECTIVE

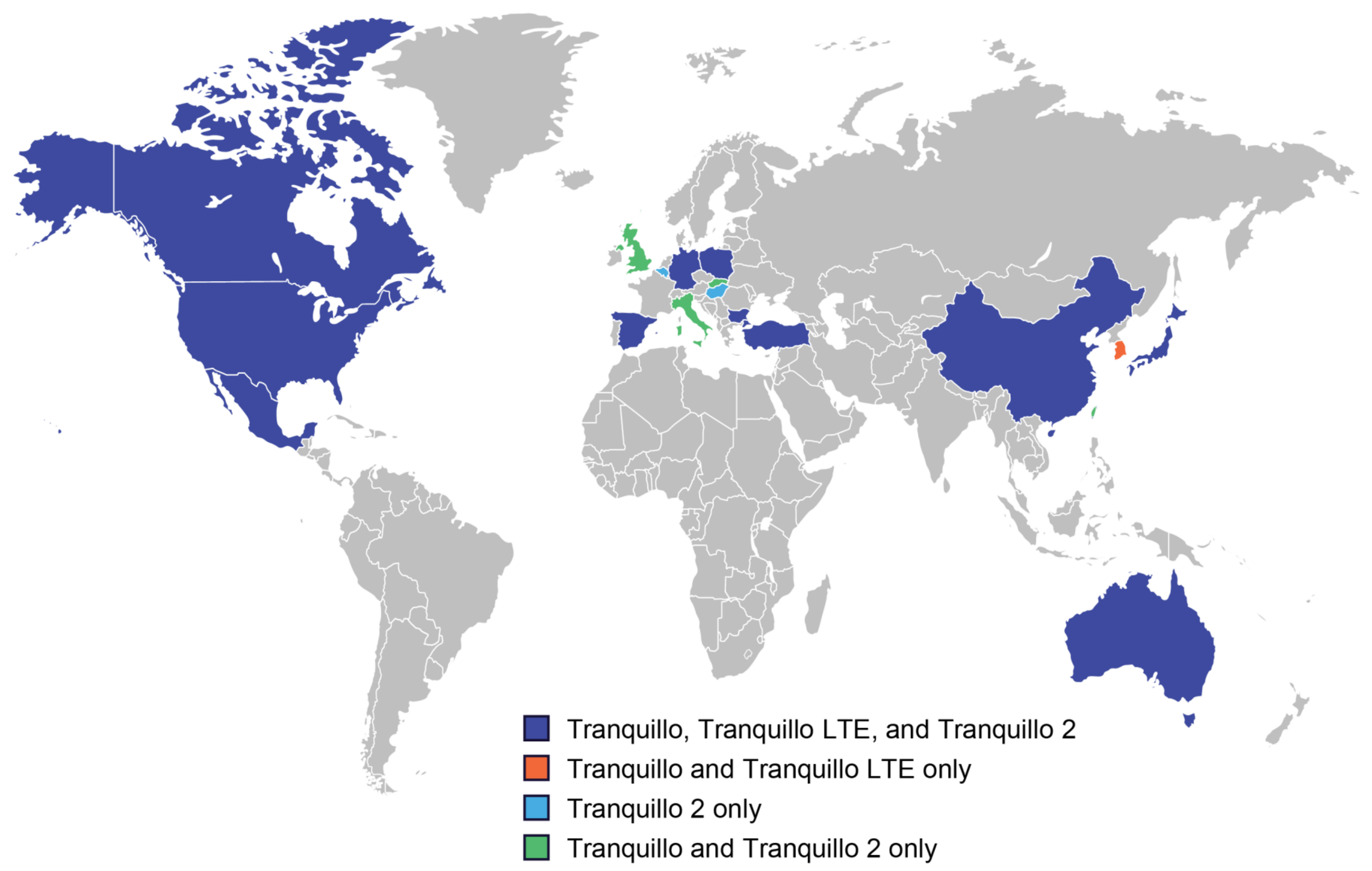
- Here, we present an overview of the Tranquillo phase 3 program, which comprises 3 phase 3 studies aiming to evaluate the efficacy, safety, and tolerability of ritlecitinib 50 mg QD and 100 mg QD in adult and adolescent participants with NSV:
  - Tranquillo (NCT05583526)
  - Tranquillo long-term extension (LTE; NCT06163326)
  - Tranquillo 2 (NCT06072183)

TRANQUILLO CLINICAL PROGRAM OVERVIEW

Locations

- The Tranquillo phase 3 program is taking place in 17 countries globally (**Figure 1**)

Figure 1. Tranquillo program locations by country



LTE, long-term extension

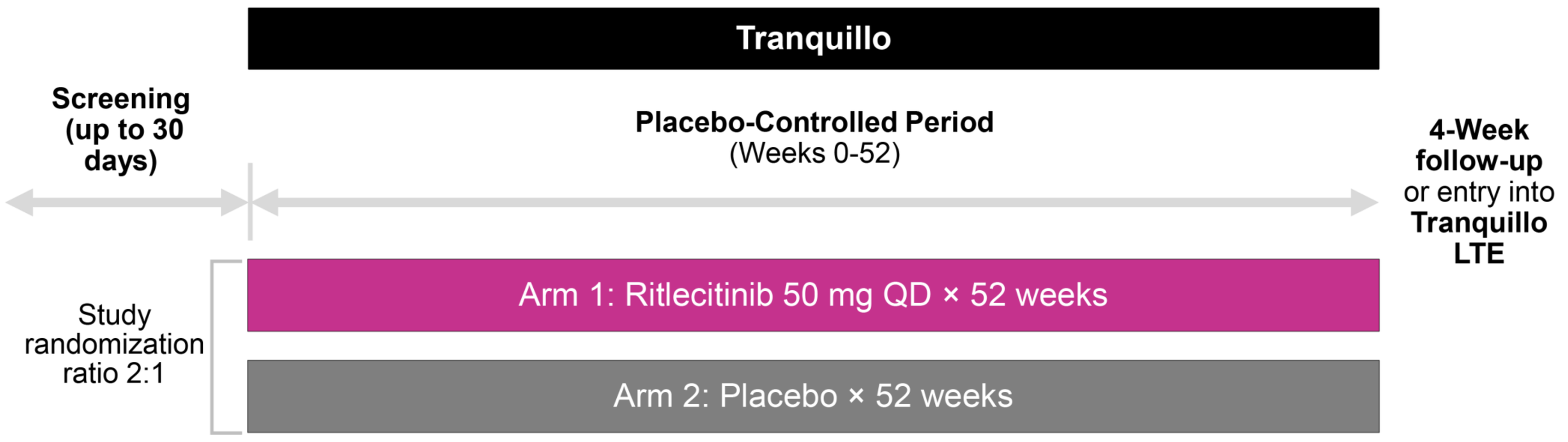
Participants

- Eligible participants include those with:
  - Age ≥12 years (Tranquillo, Tranquillo LTE)
  - Age ≥18 years (Tranquillo 2)
  - Clinical diagnosis of active or stable NSV for ≥3 months
  - Body surface area (BSA) involvement 4%-60%
  - Facial BSA ≥0.5%
  - Facial Vitiligo Area Scoring Index (F-VASI) ≥0.5
  - Total (T)-VASI ≥3

TRANQUILLO

- Tranquillo (NCT05583526) is a randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of ritlecitinib 50 mg QD vs placebo over 52 weeks (**Figure 2**)
  - Randomization will stratify participants by Fitzpatrick skin type (I/II, III/IV, and V/VI)
  - Tranquillo started on December 1, 2022
  - This study will enroll approximately 600 participants from approximately 115 locations globally

Figure 2. Study design for the Tranquillo clinical trial



LTE, long-term extension; QD, once-daily.

- Primary and (key) secondary endpoints are listed in **Table 1**

Table 1. Endpoints for the Tranquillo clinical trial

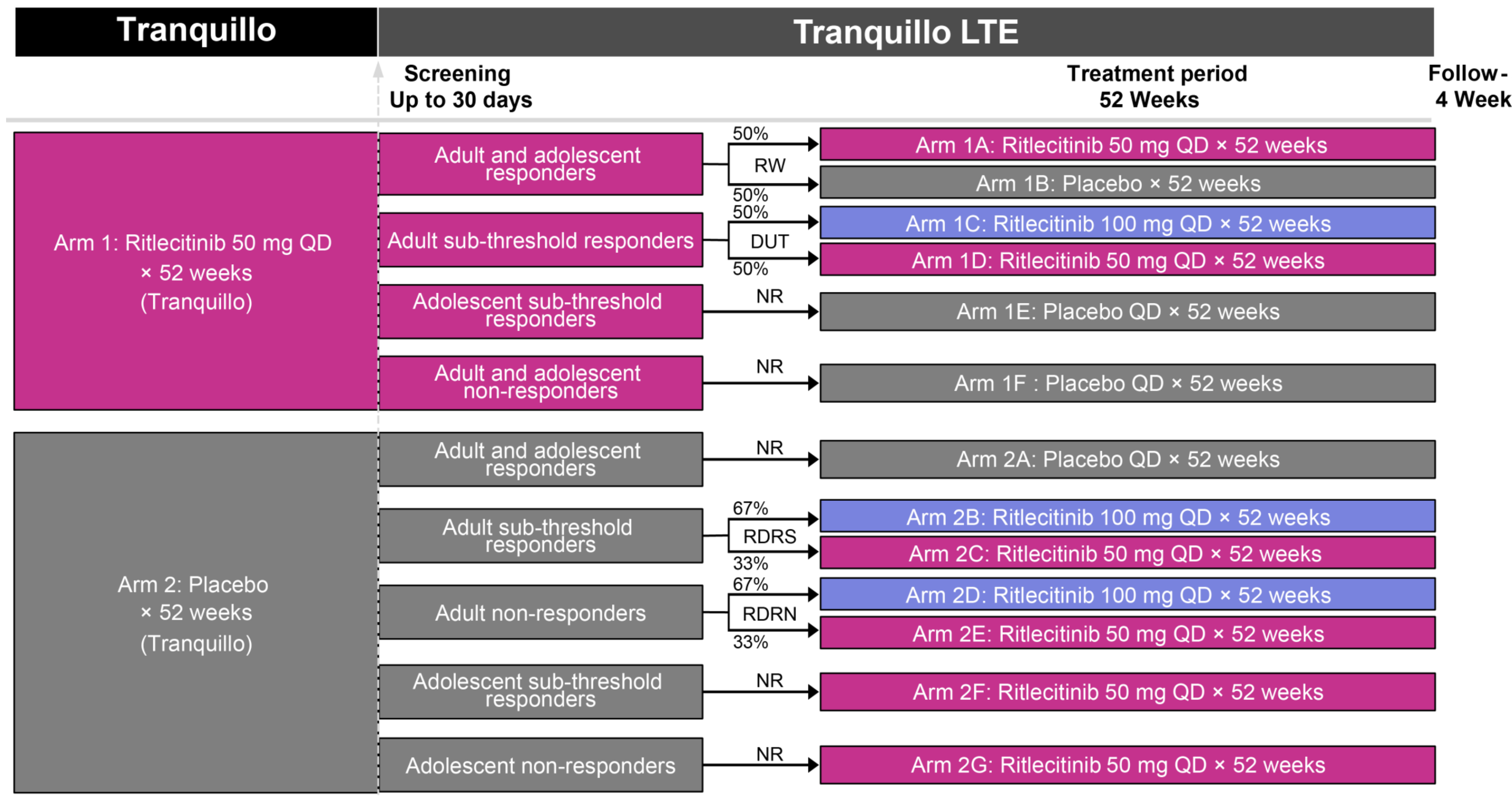
US Co-Primary Efficacy Endpoints		Global (other than US) Primary Efficacy Endpoint	
F-VASI75*	Week 52	F-VASI75*	Week 52
T-VASI50*	Week 52		
All Countries Primary Endpoint			
Safety		Throughout study	
US Key Secondary Endpoints		**Global (other than US) Key Secondary Endpoints**	
F-VASI75*	Weeks 24 and 36	F-VASI75*	Weeks 24 and 36
T-VASI50*	Weeks 24 and 36	T-VASI50*	Weeks 24, 36, and 52
%CFB in F-VASI/T-VASI	Weeks 24, 36, and 52	%CFB in F-VASI/T-VASI	Weeks 24, 36, and 52
T-VASI75*	Week 52	PGIS-F/PGIS-V†	Weeks 24, 36, and 52
PGIS-F/PGIS-V†	Week 52		

CFB, change from baseline; F-VASI, Facial Vitiligo Area Scoring Index; F-VASI75, ≥75% improvement on F-VASI from baseline; T-VASI, Total Vitiligo Area Scoring Index; T-VASI50, ≥50% improvement in T-VASI from baseline.
*Proportion of participants achieving this measurement. †Participants achieving PGIS-F/PGIS-V response, which is defined as a 1-point improvement in facial/total body vitiligo in participants with mild, moderate, or severe facial/total body vitiligo at baseline or a 2-point improvement in participants with very severe facial/total body vitiligo at baseline.

TRANQUILLO LTE

- Tranquillo LTE (NCT06163326) is a 52-week, double-blind, randomized withdrawal, dose-up titration study, investigating the safety, tolerability, and efficacy of ritlecitinib 50 mg QD and 100 mg QD and durability of response of ritlecitinib 50 mg QD following participant participation in Tranquillo (**Figure 3**)
  - Tranquillo LTE started on January 1, 2024
  - This study will enroll approximately **400 participants** who completed the Tranquillo study globally

Figure 3. Study design for the Tranquillo LTE clinical trial


Tranquillo
Tranquillo LTE
Screening Up to 30 days
Treatment period 52 Weeks
Follow-Up 4 Weeks
Arm 1: Ritlecitinib 50 mg QD × 52 weeks (Tranquillo)
Arm 2: Placebo × 52 weeks (Tranquillo)
Adult and adolescent responders
Adult sub-threshold responders
Adolescent sub-threshold responders
Adult and adolescent non-responders
Adult and adolescent responders
Adult sub-threshold responders
Adult non-responders
Adolescent sub-threshold responders
Adolescent non-responders
50%
RW
50%
50%
DUT
50%
NR
NR
NR
67%
RDRS
33%
67%
RDRN
33%
NR
NR
Arm 1A: Ritlecitinib 50 mg QD × 52 weeks
Arm 1B: Placebo × 52 weeks
Arm 1C: Ritlecitinib 100 mg QD × 52 weeks
Arm 1D: Ritlecitinib 50 mg QD × 52 weeks
Arm 1E: Placebo QD × 52 weeks
Arm 1F : Placebo QD × 52 weeks
Arm 2A: Placebo QD × 52 weeks
Arm 2B: Ritlecitinib 100 mg QD × 52 weeks
Arm 2C: Ritlecitinib 50 mg QD × 52 weeks
Arm 2D: Ritlecitinib 100 mg QD × 52 weeks
Arm 2E: Ritlecitinib 50 mg QD × 52 weeks
Arm 2F: Ritlecitinib 50 mg QD × 52 weeks
Arm 2G: Ritlecitinib 50 mg QD × 52 weeks

DUT, dose-up titration; LTE, long-term extension; NR, nonrandomized; QD, once-daily; RDRN, randomized dose-ranging nonresponders; RDRS, randomized dose-ranging subthreshold responders; RW, randomized withdrawal.

- Primary and secondary endpoints are listed in **Table 2**
- Secondary endpoints include %CFB in F-VASI and T-VASI and the proportion of patients achieving F-VASI50/75/90/100 and T-VASI50/75/90/100 at Weeks 4, 8, 12, 24, 36, and 52

Table 2. Endpoints for the Tranquillo LTE clinical trial

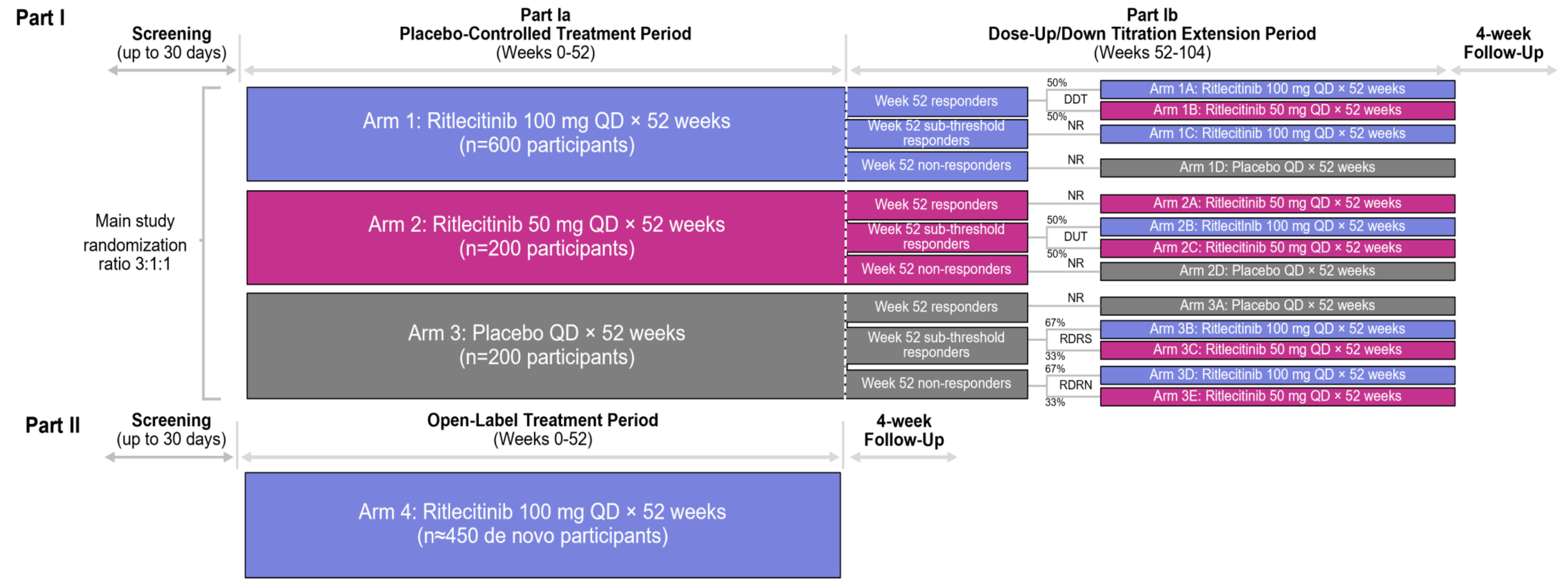
Endpoints	
Safety	Throughout study
Secondary Endpoints	
T-VASI75/50/90/100*	Weeks 4, 8, 12, 24, 36, and 52
F-VASI75/50/90/100*	Weeks 4, 8, 12, 24, 36, and 52
%CFB in F-VASI/T-VASI	Weeks 4, 8, 12, 24, 36, and 52
PGIS-F/PGIS-V†	Weeks 24, 36, and 52

F-VASI, Facial Vitiligo Area Scoring Index; F-VASI75, ≥75% improvement on F-VASI from baseline; PGIS-F, Patient Global Impression of Severity – Face; PGIS-V, Patient Global Impression of Severity – Overall Vitiligo; T-VASI, Total Vitiligo Area Scoring Index; T-VASI50, ≥50% improvement in T-VASI from baseline.
*Proportion of participants achieving this measurement. †Participants achieving PGIS-F/PGIS-V response, which is defined as a 1-point improvement in facial/total body vitiligo in participants with mild, moderate, or severe facial/total body vitiligo at baseline or a 2-point improvement in participants with very severe facial/total body vitiligo at baseline.

TRANQUILLO 2

- Tranquillo 2 (NCT06072183) started on November 8, 2023 and contains two parts:
- Part I
  - 52-week randomized, double-blind, placebo-controlled study comparing ritlecitinib 50 mg QD and 100 mg QD vs placebo (**Figure 4**)
  - 52-week extension with randomized dose-up/dose-down titration
  - The study will enroll approximately 1000 participants in Part I from approximately 230 locations globally
  - Participants will be stratified by Fitzpatrick skin type (I/II, III/IV, V/VI)
- Part II
  - De novo 52-week nonrandomized, open-label ritlecitinib 100 mg QD arm to support safety data
  - Part II will enroll simultaneously an additional approximately **450 de novo participants**

Figure 4. Study design for the Tranquillo 2 clinical trial


Part I
Screening (up to 30 days)
Part Ia Placebo-Controlled Treatment Period (Weeks 0-52)
Part Ib Dose-Up/Down Titration Extension Period (Weeks 52-104)
4-week Follow-Up
Main study randomization ratio 3:1:1
Arm 1: Ritlecitinib 100 mg QD × 52 weeks (n=600 participants)
Arm 2: Ritlecitinib 50 mg QD × 52 weeks (n=200 participants)
Arm 3: Placebo QD × 52 weeks (n=200 participants)
Week 52 responders
Week 52 sub-threshold responders
Week 52 non-responders
50%
DDT
50%
NR
NR
NR
50%
DUT
50%
NR
NR
67%
RDRS
33%
67%
RDRN
33%
Arm 1A: Ritlecitinib 100 mg QD × 52 weeks
Arm 1B: Ritlecitinib 50 mg QD × 52 weeks
Arm 1C: Ritlecitinib 100 mg QD × 52 weeks
Arm 1D: Placebo QD × 52 weeks
Arm 2A: Ritlecitinib 50 mg QD × 52 weeks
Arm 2B: Ritlecitinib 100 mg QD × 52 weeks
Arm 2C: Ritlecitinib 50 mg QD × 52 weeks
Arm 2D: Placebo QD × 52 weeks
Arm 3A: Placebo QD × 52 weeks
Arm 3B: Ritlecitinib 100 mg QD × 52 weeks
Arm 3C: Ritlecitinib 50 mg QD × 52 weeks
Arm 3D: Ritlecitinib 100 mg QD × 52 weeks
Arm 3E: Ritlecitinib 50 mg QD × 52 weeks
Part II
Screening (up to 30 days)
Open-Label Treatment Period (Weeks 0-52)
4-week Follow-Up
Arm 4: Ritlecitinib 100 mg QD × 52 weeks (n≈450 de novo participants)

DDT, dose-down titration; DUT, dose-up titration; NR, nonrandomized; QD, once-daily; RDRN, randomized dose-ranging nonresponders; RDRS, randomized dose-ranging subthreshold responders; RW, randomized withdrawal.

- Primary and (key) secondary endpoints are listed in **Table 3**

Table 3. Endpoints for the Tranquillo 2 clinical trial

US Co-Primary Efficacy Endpoints		Global (other than US) Primary Efficacy Endpoint	
F-VASI75*	Week 52	F-VASI75*	Week 52
T-VASI50*	Week 52		
All Countries Primary Endpoint			
Safety		Throughout study	
US Key Secondary Endpoints		**Global (other than US) Key Secondary Endpoints**	
F-VASI75*	Weeks 24 and 36	F-VASI75*	Weeks 24 and 36
T-VASI50*	Weeks 24 and 36	T-VASI50*	Weeks 24, 36, and 52
%CFB in F-VASI/T-VASI	Weeks 24, 36, and 52	%CFB in F-VASI/T-VASI	Weeks 24, 36, and 52
T-VASI75*	Week 52	PGIS-F/PGIS-V†	Weeks 24, 36, and 52
PGIS-F/PGIS-V†	Week 52		

CFB, change from baseline; F-VASI, Facial Vitiligo Area Scoring Index; F-VASI75, ≥75% improvement on F-VASI from baseline; PGIS-F, Patient Global Impression of Severity – Face; PGIS-V, Patient Global Impression of Severity – Overall Vitiligo; T-VASI, Total Vitiligo Area Scoring Index; T-VASI50, ≥50% improvement in T-VASI from baseline.
*Proportion of participants achieving this measurement. †Participants achieving PGIS-F/PGIS-V response, which is defined as a 1-point improvement in facial/total body vitiligo in participants with mild, moderate, or severe facial/total body vitiligo at baseline or a 2-point improvement in participants with very severe facial/total body vitiligo at baseline.

HIGHLIGHTS

- Ritlecitinib is a targeted systemic treatment currently under investigation for treatment of NSV
- The Tranquillo program aims to evaluate the efficacy, safety, and tolerability of ritlecitinib 100 mg QD or 50 mg QD in patients with NSV
- Overall, the Tranquillo program will examine a large cohort of approximately **2050 patients with NSV** over the course of up to **104 weeks**

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DISCLOSURES

TL, PG, LN, and CW are employees of and hold stock or stock options in Pfizer Inc. RA is an employee of and holds stock or stock options in Pfizer Pharmaceutical Israel LTD. IH is a consultant for AbbVie, Pfizer, Incyte, UCB, Boehringer Ingelheim, Sonoma, Merck, Union Therapeutics, Novartis, Jansen, Avita, Galderma, Vimela, and Almirall; an investigator for Lenicura, Pfizer, Incyte, Avita, L'Oréal/La Roche-Posay, ITN, and AbbVie; and a board member and past president of the Hidradenitis Suppurativa and Global Vitiligo foundations. RS has been an investigator for and/or provided professional services to AbbVie, Aerotek Scientific, Akeso Biopharma, Amgen, Arcutis, Arena Pharmaceuticals, Ascend Laboratories, AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus BioSciences, Connect Biopharma, Cutanea, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, LEO Pharma, MedImmune/ AstraZeneca, Merck Sharp & Dohme, Novartis, Oncobiologics, Pfizer, Regeneron, Reistone Biopharma, Roche, Samson Medical Technologies, Sanofi, Sun Pharma, and UCB Pharma. DR has served as a consultant for, spoken for, or conducted trials for the following companies: AbbVie, Abcuro, AltruBio, Amgen, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Concert, CSL Behring, Dermavant, Dermira, Galderma, Incyte, Janssen, Kyowa Kirin, Lilly, Merck, Nektar, Novartis, Pfizer, RAPT, Regeneron, Recludix, Revolo Biotherapeutics, Sanofi, Sun Pharmaceuticals, UCB, Viela Bio, and Zura Bio. KE is a consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. LX, KS, and DP declare no interests.

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