Repibresib (VYN201) Phase 2b Topline Results

Repibresib in Subjects with Non-segmental Vitiligo

July 2025

VYNE™ THERAPEUTICS

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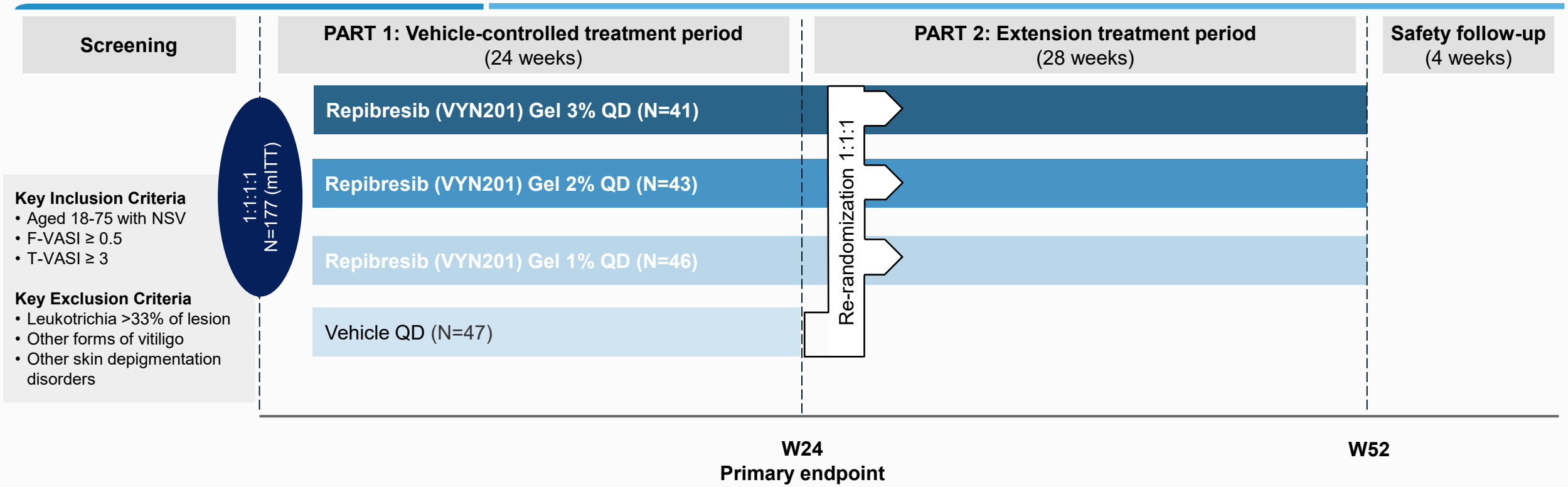
Repibresib (VYN201) Phase 2b NSV Trial Design

Top-line results from 24-week vehicle-controlled treatment period reported



Key Inclusion Criteria
- Aged 18-75 with NSV
- F-VASI ≥ 0.5
- T-VASI ≥ 3

Key Exclusion Criteria
- Leukotrichia >33% of lesion
- Other forms of vitiligo
- Other skin depigmentation disorders

Key safety assessments:

- Treatment emergent adverse events
- Local skin tolerability assessments
- Clinical laboratory assessments, Physical exam/vitals, PK

Key efficacy endpoints:

Primary: Proportion of subjects achieving F-VASI50 at Week 24 vs. Vehicle
Secondary: Proportion of subjects achieving T-VASI50 at Week 52
Proportion of subjects achieving F-VASI25/75 at Week 24 and 52
% CFB in F-VASI score at Week 24 and 52

Key Patient Demographics: Baseline Characteristics Were Generally Balanced Between Treatment Arms

Characteristics (mITT)	Repibresib 3% (N=41)	Repibresib 2% (N=43)	Repibresib 1% (N=46)	Vehicle (N=47)	Total (N=177)
Age, mean (SD), y	49.0 (9.97)	51.4 (14.04)	48.6 (12.24)	51.7 (13.17)	50.2 (12.46)
Age Category (years)					
≤ 40	6 (14.6)	8 (18.6)	13 (28.3)	11 (23.4)	38 (21.5)
> 40 to 65	34 (82.9)	30 (69.8)	29 (63.0)	29 (61.7)	122 (68.9)
> 65	1 (2.4)	5 (11.6)	4 (8.7)	7 (14.9)	17 (9.6)
Female, n (%)	25 (61.0)	19 (44.2)	21 (45.7)	27 (57.4)	92 (52.0)
White, n (%)	34 (82.9)	38 (88.4)	34 (73.9)	36 (76.6)	142 (80.2)
Fitzpatrick Skin Type, n (%)					
I	1 (2.4)	3 (7.0)	0	3 (6.4)	7 (4.0)
II	12 (29.3)	13 (30.2)	16 (34.8)	12 (25.5)	53 (29.9)
III	13 (31.7)	16 (37.2)	17 (37.0)	17 (36.2)	63 (35.6)
IV	11 (26.8)	10 (23.3)	11 (23.9)	10 (21.3)	42 (23.7)
V	3 (7.3)	1 (2.3)	2 (4.3)	4 (8.5)	10 (5.6)
VI	1 (2.4)	0	0	1 (2.1)	2 (1.1)
Baseline F-VASI, mean (SD)	0.8807 (0.5230)	0.8697 (0.5323)	0.8286 (0.4266)	0.9006 (0.4478)	0.8698 (0.4790)
Baseline T-VASI, mean (SD)	6.2866 (1.9979)	6.1232 (2.2811)	6.2016 (2.2660)	6.0913 (2.2728)	6.1730 (2.1949)
F-BSA, mean (SD), %	1.0334 (0.5976)	0.9898 (0.5867)	0.9320 (0.5007)	1.0193 (0.5312)	0.9927 (0.5502)
T-BSA, mean (SD), %	7.0583 (1.9929)	6.6817 (2.2868)	6.5912 (2.3862)	6.6120 (2.4283)	6.7269 (2.2764)
Disease Activity (Face), (%)					
Progressive	21 (51.2)	16 (37.2)	15 (32.6)	16 (34.0)	68 (38.4)
Stable	20 (48.8)	27 (62.8)	31 (67.4)	31 (66.0)	109 (61.6)

Subject Disposition & Treatment Discontinuation During 24-Week Period

	Repibresib 3%	Repibresib 2%	Repibresib 1%	Vehicle	Repibresib Overall	Tota l
Intent to Treat (ITT)	50	51	51	52	152	204
Modified Intent to Treat (mITT)	41	43	46	47	130	177
Per Protocol (PP)	40	43	46	47	129	176
Events/PRs						
Discontinued before Week 24 (mITT)	**15 (36.6%)**	**13 (30.2%)**	**12 (26.1%)**	**5 (10.6%)**	**40 (30.7%)**	**45 (25.4%)**
Patient Decision	9 (22.0%)	5 (11.6%)	3 (5.9%)	2 (4.3%)	17 (13.1%)	19 (10.7%)
Lost to Follow-up	1 (2.4%)	5 (11.6%)	6 (11.8%)	2 (4.3%)	12 (9.2%)	14 (7.9%)
Adverse Event	3 (7.3%)	2 (4.7%)	3 (5.9%)	0	8 (6.2%)	8 (4.5%)
Non-Compliance with Study Procedure	1 (2.4%)	0	0	0	1 (0.8%)	1 (0.5%)
Lack of efficacy to study treatment	1 (2.4%)	0	0	1 (2.1%)	2 (1.5%)	2 (1.1%)
Protocol deviation	0	1 (2.3%)	0	0	1 (0.8%)	1 (0.5%)

- mITT reflects exclusion of 2 non-compliant sites in Canada & 3 additional subjects with FVASI <0.5 at Baseline
- Overall discontinuation rates for all repibresib arms higher than treatment arms in Phase 2b and Phase 3 studies for approved and late-stage vitiligo therapies*
- Discontinuation rates due to AEs for all repibresib arms comparable to treatment arms in Phase 2b and Phase 3 studies for approved and late-stage vitiligo therapies *

*Clinicaltrials.gov; Study Publications; 1. NCT03715829; 2. NCT04818346; NCT03099304; NCT04927975

Efficacy Endpoints: F-VASI50 (Primary) and F-VASI75 (Key Secondary)

24-week vehicle-controlled treatment period, mITT

Proportion of Subjects Achieving F-VASI50 at Week 24*

Variable	Repibresib 3% (N=41)	Repibresib 2% (N=43)	Repibresib 1% (N=46)	Vehicle (N=47)
Subjects Achieving F-VASI50 at Week 24				
Responder	8/41 (19.5%)	7/43 (16.3%)	8/46 (17.4%)	11/47 (23.4%)
Non-Responder	14/41 (34.1%)	20/43 (46.5%)	25/46 (54.3%)	29/47 (61.7%)
Imputed Population	19/41 (46.3%)	16/43 (37.2%)	13/46 (28.3%)	7/47 (14.9%)
Odds Ratio	2.21	1.26	0.98	
95% Confidence Interval	(0.8, 6.08)	(0.46, 3.45)	(0.36, 2.71)	
P-Value	0.1245	0.6497	0.9718	

Proportion of Subjects Achieving F-VASI75 at Week 24*

Variable	Repibresib 3% (N=41)	Repibresib 2% (N=43)	Repibresib 1% (N=46)	Vehicle (N=47)
Subjects Achieving F-VASI75 at Week 24				
Responder	4/41 (9.8%)	3/43 (7.0%)	5/46 (10.9%)	3/47 (6.4%)
Non-Responder	18/41 (43.9%)	24/43 (55.8%)	28/46 (60.9%)	37/47 (78.7%)
Imputed Population	19/41 (46.3%)	16/43 (37.2%)	13/46 (28.3%)	7/47 (14.9%)
Odds ratio	3.12	1.97	2.22	
95% Confidence Interval	(0.67, 14.54)	(0.39, 9.85)	(0.50, 9.92)	
P-Value	0.1468	0.4096	0.2946	

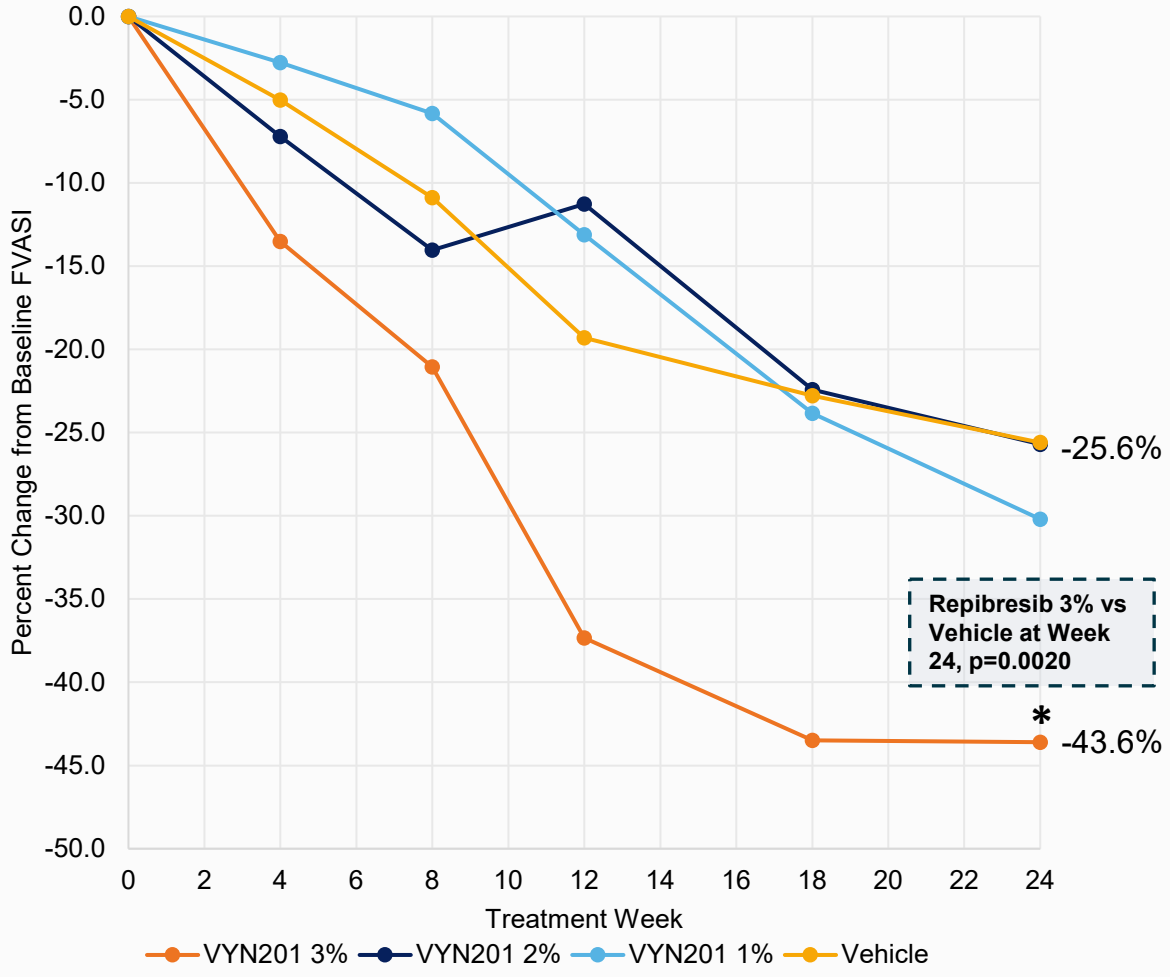
- Per Protocol sensitivity analysis was consistent with the above
- Imputed population = Discontinued subjects and subjects excluded from the primary population as due to an out of window visit at Week 24. This included n=2 F-VASI50 responders receiving Repibresib 3% and n=1 F-VASI50 responder receiving Repibresib 2%.

* Logistic Regression, Multiple Imputation

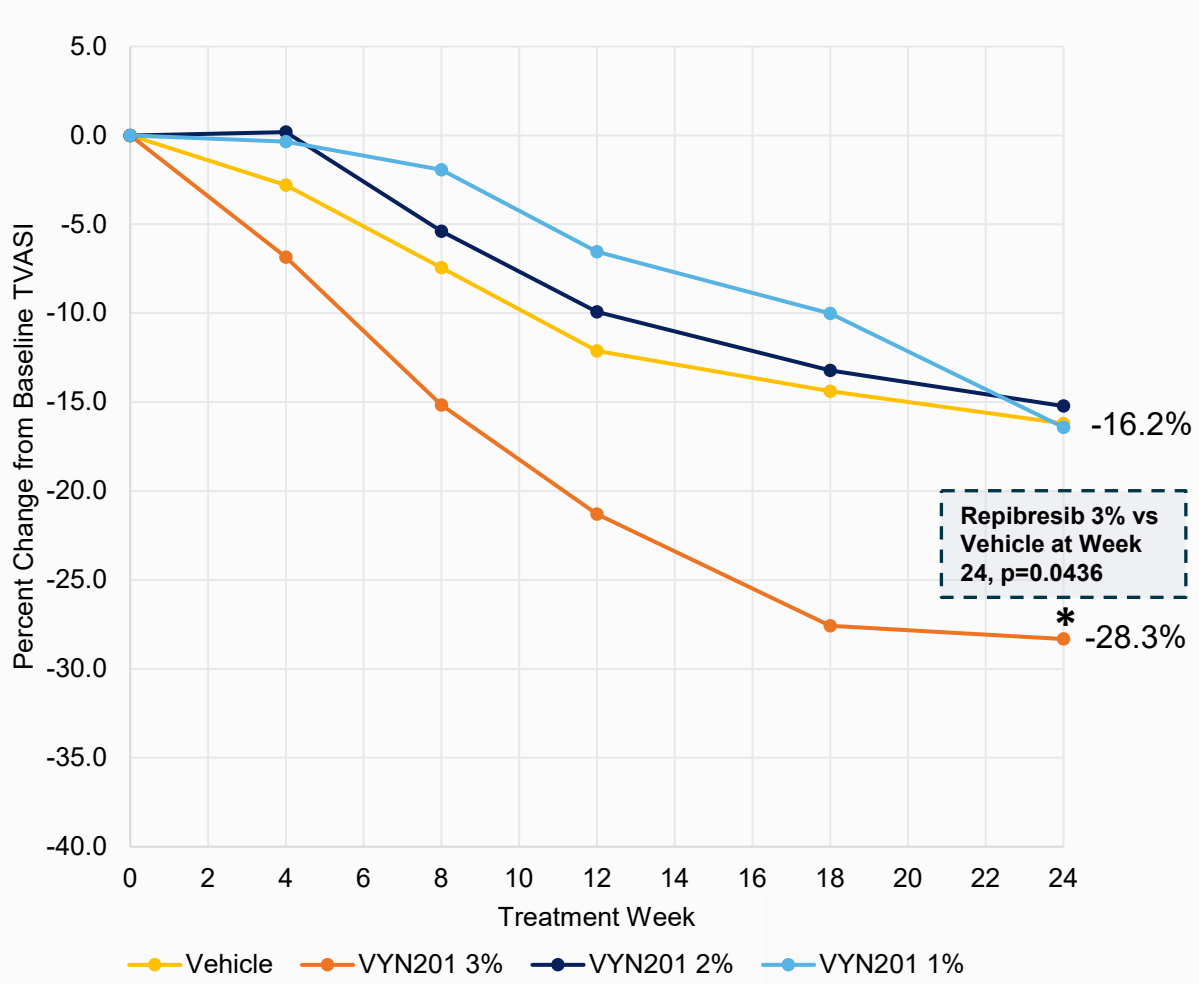
Efficacy Endpoints: % Change from BL in F-VASI (Key Secondary) & T-VASI (Exploratory)

24-week vehicle-controlled treatment period, mITT

Change from Baseline in F-VASI by Week*



Change from Baseline in T-VASI by Week*



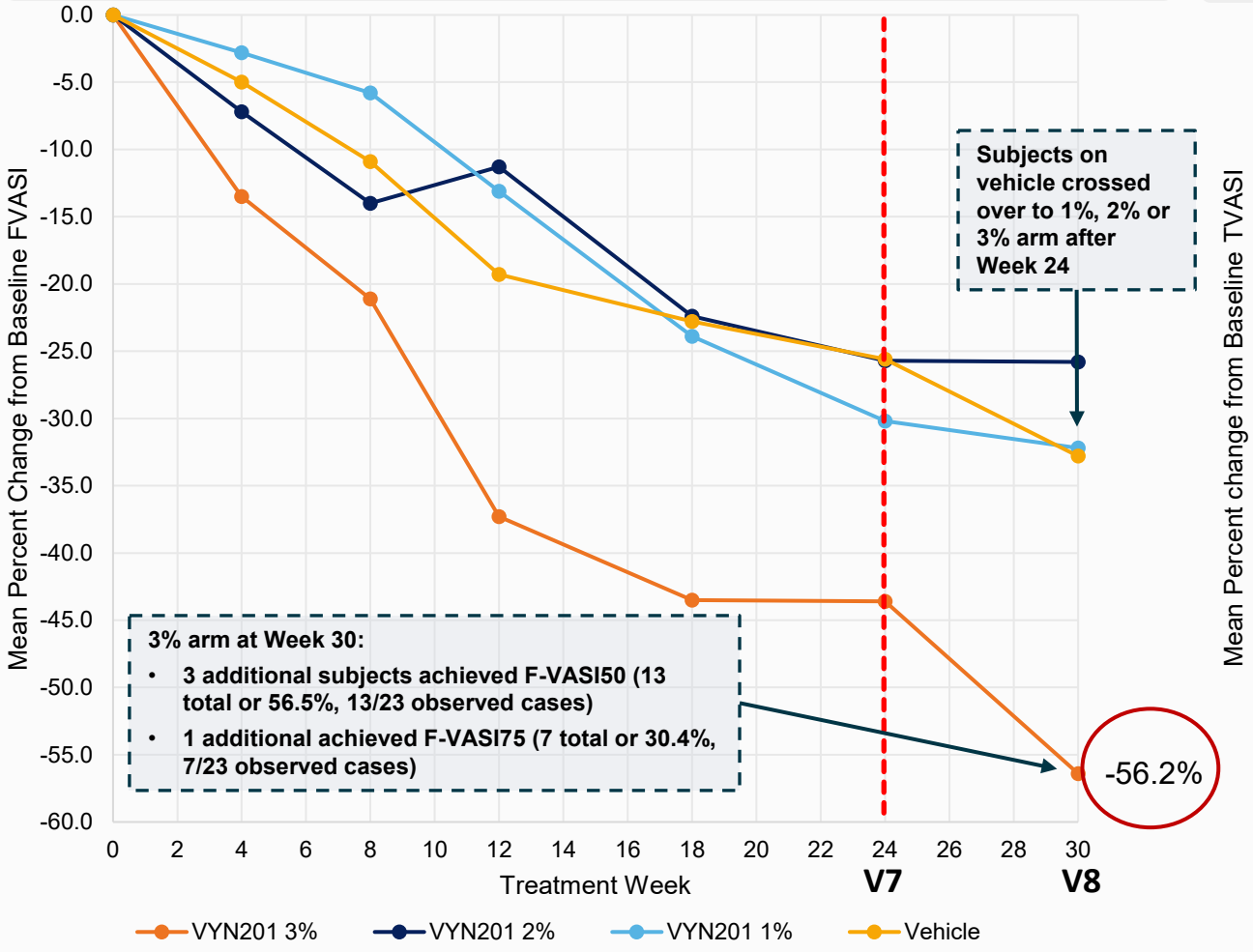
*ANCOVA, LSMean, Observed Case Data

Additional Exploratory Analyses: F-VASI and T-VASI Change beyond Week 24

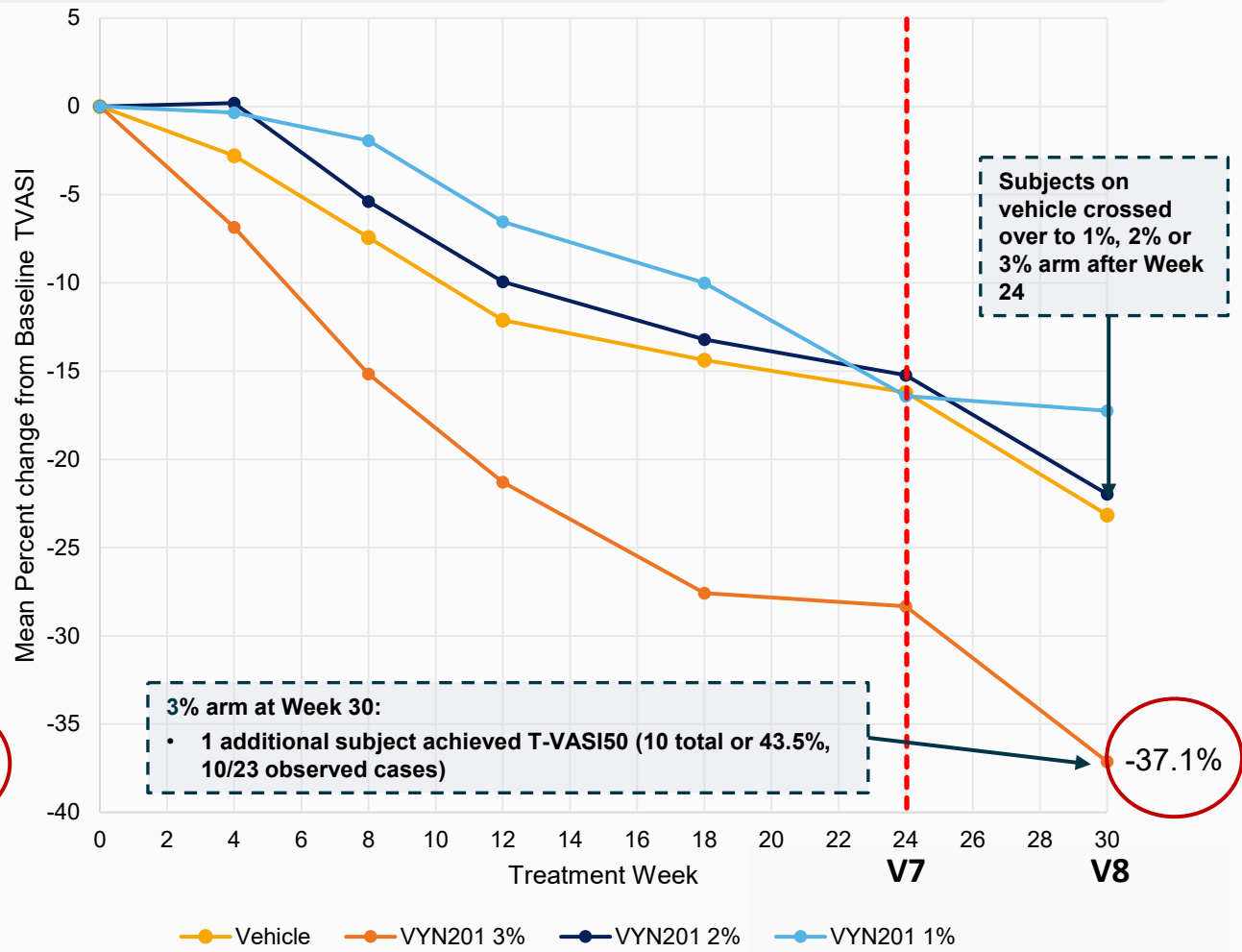
96% of subjects that reached Week 24 visit continued into the extension

3% dose continued to show deepening of effect from Visit 7 (Week 24) to Visit 8 (Week 30)

Change from Baseline in F-VASI by Week (Observed Cases, mITT)



Change from Baseline in T-VASI by Week (Observed Cases, mITT)



Part 2

Preliminary Week 30 data as of 25JUL25

Summary of Treatment Emergent Adverse Events ≥5% Frequency

24-week vehicle-controlled treatment period

Majority of skin-related* TEAEs were mild in severity and resolved during study conduct (76.0% “Mild”, 23.7% “Moderate” and 0.2% “Severe”)

Adverse Events ≥5% Frequency, n (%)	3% Repibresib (n=50)	2% Repibresib (n=51)	1% Repibresib (n=51)	Vehicle (n=52)	Total (n=204)
Patients with at least one TEAE	40 (80.0%)	37 (72.5%)	39 (76.5%)	23 (44.2%)	139 (68.1%)
Most common TEAEs by PT					
Application site pain	7 (14.0%)	3 (5.9%)	7 (13.7%)	2 (3.8%)	19 (9.3%)
Erythema	3 (6.0%)	7 (13.7%)	6 (11.8%)	2 (3.8%)	18 (8.8%)
Burning sensation	4 (8.0%)	6 (11.8%)	4 (7.8%)	1 (1.9%)	15 (7.4%)
Seborrhoeic dermatitis	8 (16.0%)	1 (2.0%)	3 (5.9%)	2 (3.8%)	14 (6.9%)
Dry skin	2 (4.0%)	6 (11.8%)	3 (5.9%)	2 (3.8%)	13 (6.4%)
Pruritus	0	3 (5.9%)	7 (13.7%)	3 (5.8%)	13 (6.4%)
Skin irritation	1 (2.0%)	7 (13.7%)	4 (7.8%)	0	12 (5.9%)
Rash	1 (2.0%)	6 (11.8%)	3 (5.9%)	1 (1.9%)	11 (5.4%)
Patients with serious TEAE	0	0	1 (2.0%)**	0	1 (0.5%)
Patients with TEAE leading to discontinuation	3 (6.0%)	2 (3.9%)	3 (5.9%)	0	8 (3.9)

** Acute cholelithiasis without obstruction, moderate severity, not drug related

- No clear dose-dependent increase in frequency of skin-related TEAEs
- Discontinuation rates due to AEs for all repibresib arms comparable to treatment arms in Phase 2b and Phase 3 studies for approved and late-stage vitiligo therapies

*Grouped analysis of “Skin and subcutaneous tissue disorders” and “General disorders and administration site conditions” system organ classes