Clinical safety and efficacy of RPT193, an oral CCR4 inhibitor: Results from a randomized, placebo-controlled Phase 1b monotherapy trial in patients with moderate-to-severe atopic dermatitis

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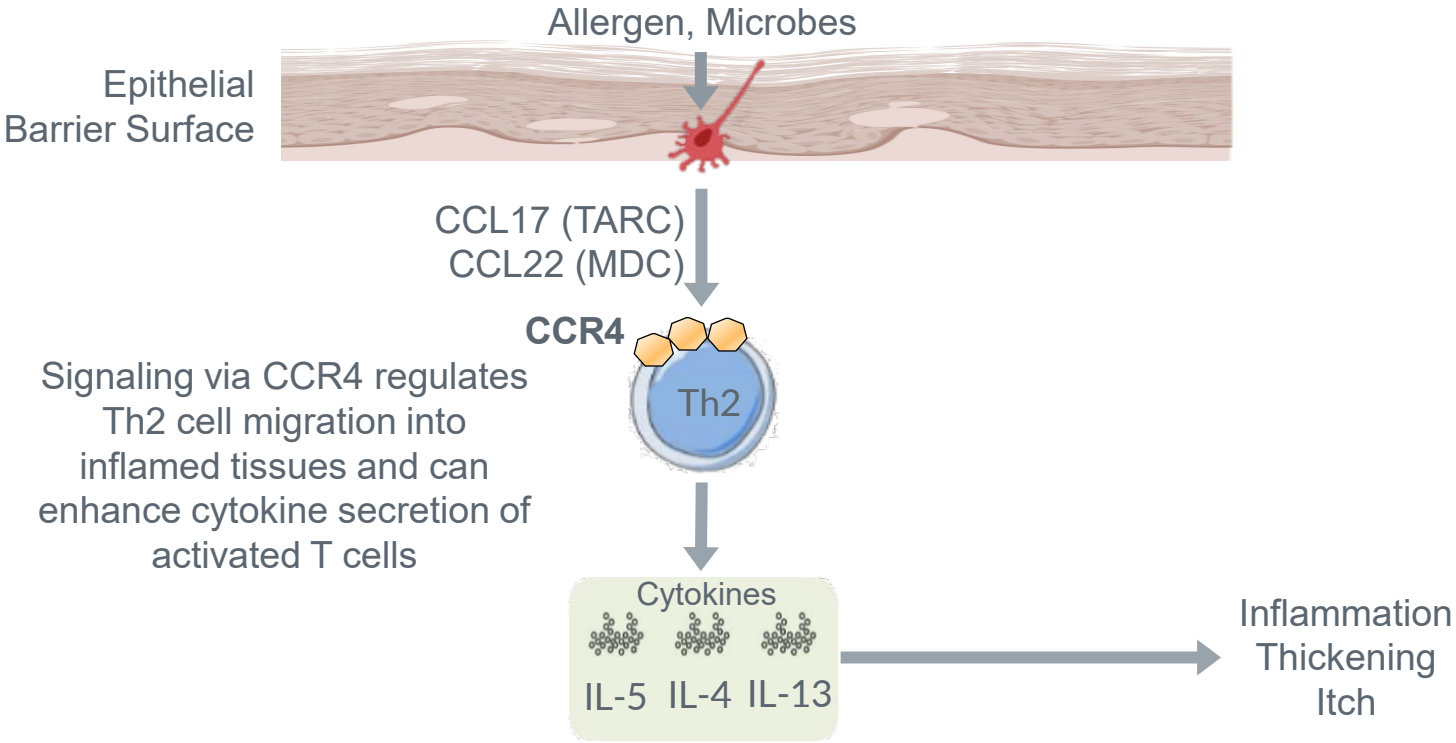
Disclosures

- R Bissonnette is an Advisory Board Member, Consultant, Speaker and/or Investigator for and receives honoraria and/or grant from AbbVie, Arcutis, Arena Pharma, Aristea, Asana BioSciences, Bellus Health, Bluefin Biomedicine, Boehringer-Ingelheim, CARA, Dermavant, Eli Lilly, EMD Serono, Evidera, Galderma, GSK, Inmagene Bio, Incyte, Kiniksa, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar, RAPT, Regeneron, Respivant, Sanofi-Genzyme, Sienna and Target RWE. R Bissonnette is also an employee and shareholder of Innovaderm Research.

RPT193 Targets Th2 Activity Responsible for Allergic Inflammation in Atopic Dermatitis, Asthma, and Other Diseases



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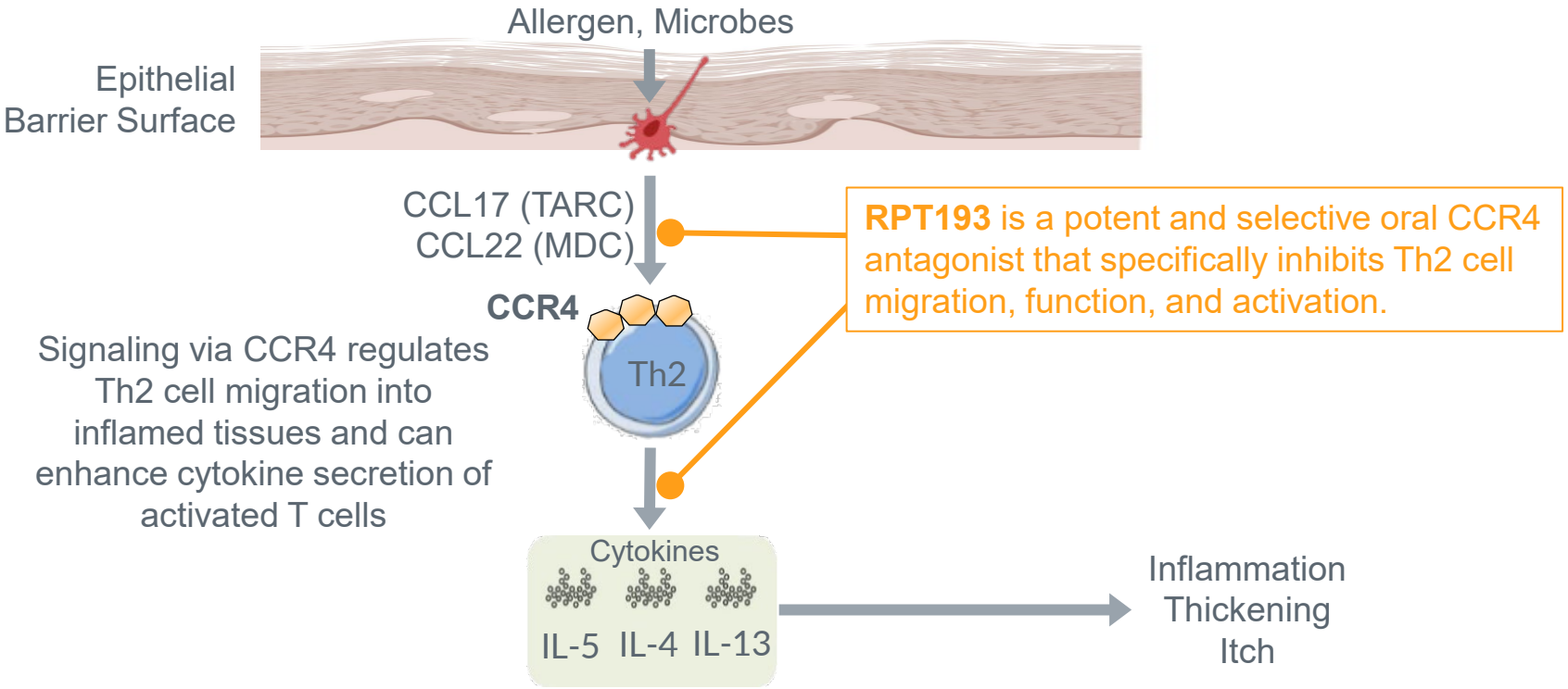
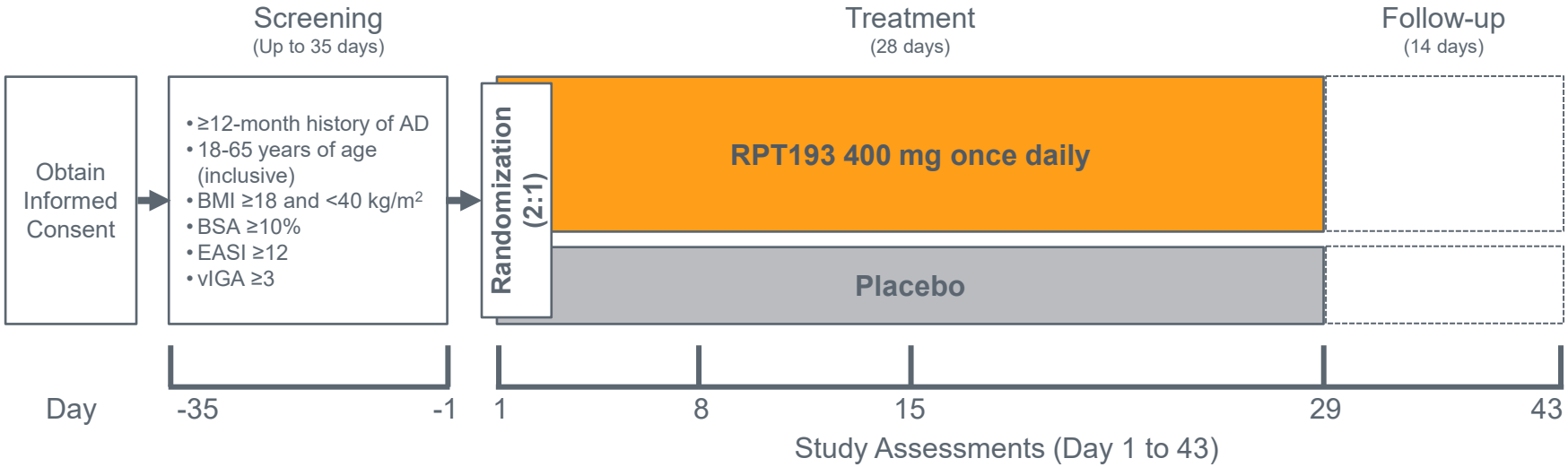
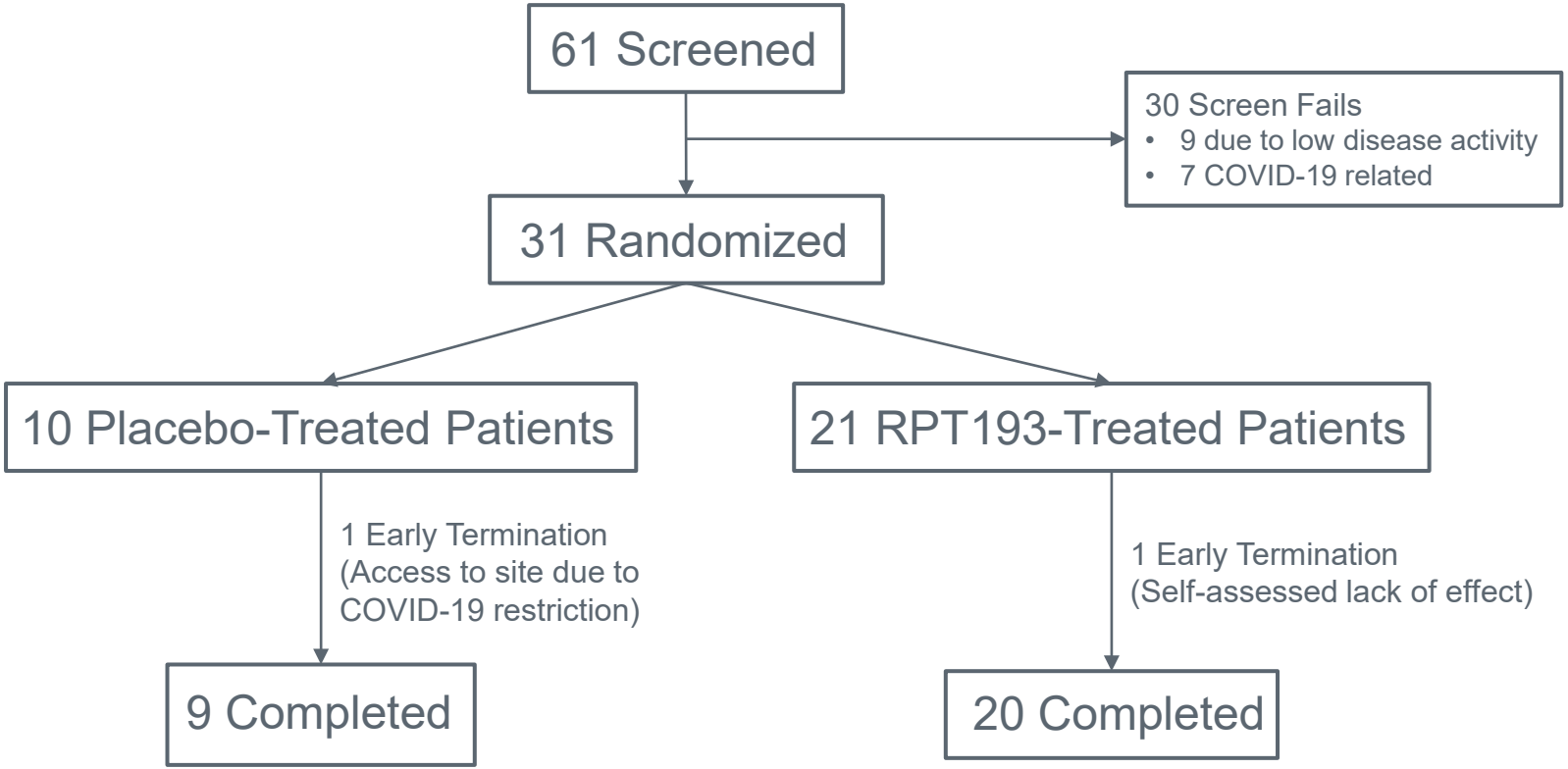


Phase 1b Trial Explored RPT193 Activity in Patients with Moderate-to-Severe Atopic Dermatitis



- Phase 1b trial part of a broader study conducted in healthy volunteers (HV) to investigate single and multiple doses of RPT193
- 400 mg dose selected based on safety, tolerability, PK and PD data from HV
- Double-blind, randomized, monotherapy study
- Primary and secondary endpoints were safety and PK, respectively
  - Trial was not powered for any specific endpoint
- Modified Intent to Treat (mITT) dataset with arithmetic means and standard error for continuous endpoints presented

Patient Disposition



Phase 1b Patient Demographics and Baseline AD Characteristics

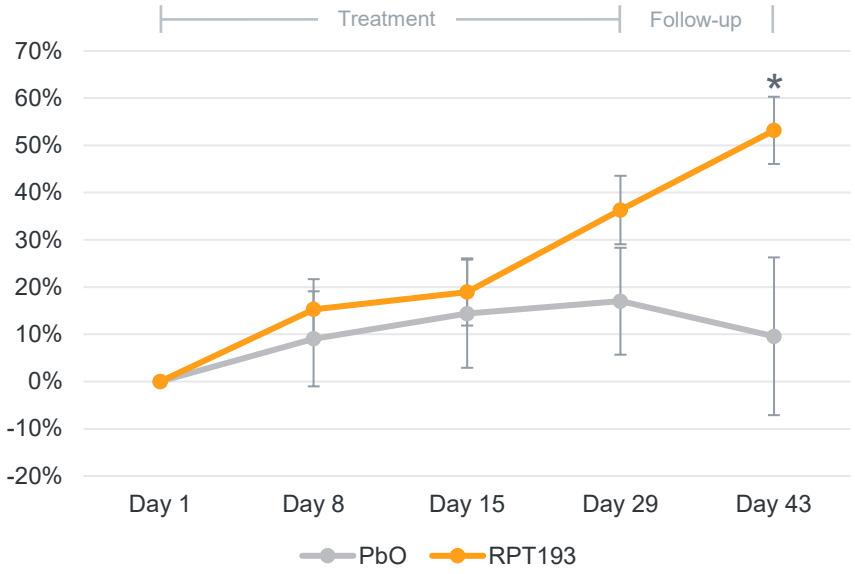
	Placebo	RPT193
N	10	21
Age, Mean (Range)	35.8 (22-64)	41.1 (19-63)
Female, n (%)	4 (40.0%)	12 (57.1%)
Hispanic or Latino Ethnicity, n (%)	3 (30.0%)	3 (14.3%)
Race		
White, n (%)	5 (50.0%)	12 (57.1%)
Asian, n (%)	0 (0%)	2 (9.5%)
Black or African American, n (%)	5 (50.0%)	7 (33.3%)
Baseline AD Characteristics		
EASI, Mean (Range)	21.07 (13.6-45.5)	18.49 (12-30)
BSA, Mean (Range)	24.50 (10-61)	23.29 (11-55)
vIGA 3, n (%)	8 (80.0%)	18 (85.7%)
Peak NRS, Mean (Range)	7.3 (3-10)	6.95 (3-10)
Peak NRS ≥4, n (%)	9 (90.0%)	20 (95.2%)

RPT193: Safety and Tolerability

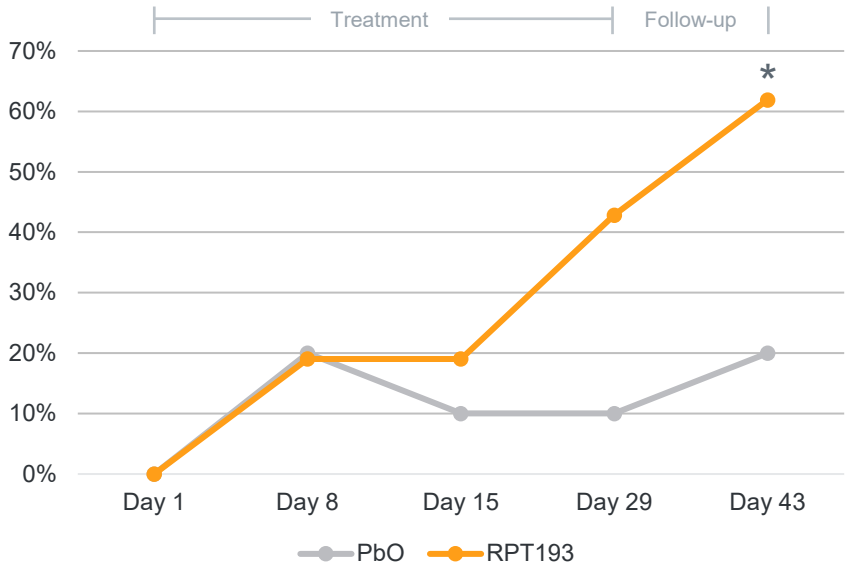
- No SAEs reported
- All TEAEs were mild or moderate
  - TEAEs reported in 42.9% of subjects in the RPT193 arm and 20% of patients in the placebo arm
  - All TEAEs in the RPT193 arm resolved with most resolving during treatment
- Only one TEAE reported by more than one patient
  - 3 patients (14.3%) in the RPT193 arm reported nausea
    - None required treatment
    - No effect on ability to tolerate a full course of treatment
    - Most were self-limited and resolved within the first five days
    - Nausea observed in 12.5% of HV in the placebo arm of the MAD portion of the Phase 1
- No laboratory safety signals, ECG changes, or vital sign changes of clinical significance noted
- No serious infections, acne, conjunctivitis, or hematologic AEs observed
- No study discontinuations due to adverse events
- One case of early treatment discontinuation in the RPT193 arm on the final day of dosing (day 28) due to an asymptomatic exanthem that was preceded by arthralgias and accompanied by dysgeusia (loss of sense of taste)

RPT193: Percent Improvement in EASI and EASI-50

% Improvement in EASI

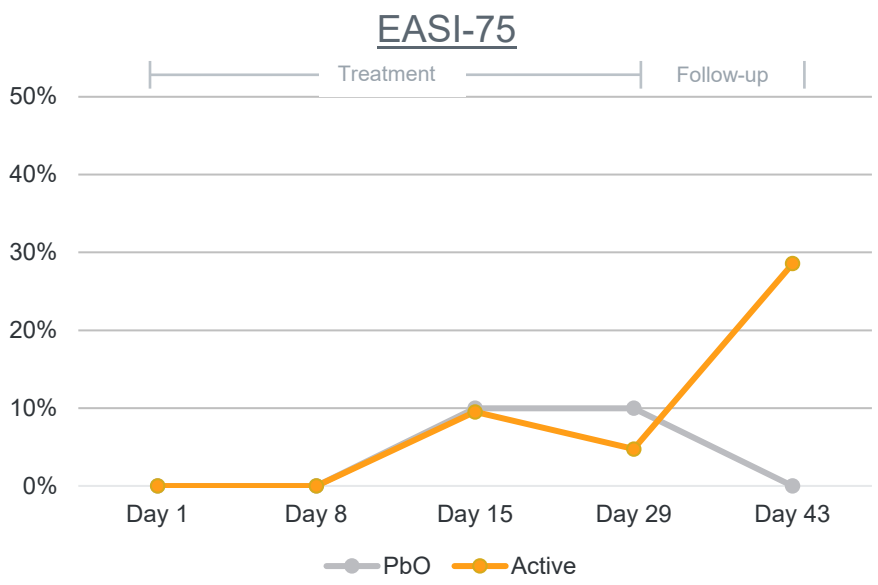


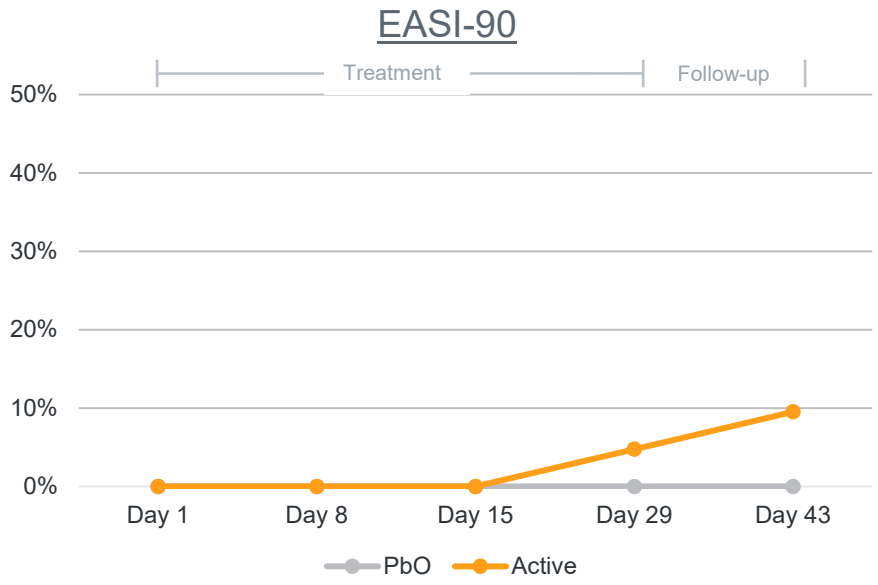
Proportion of EASI-50



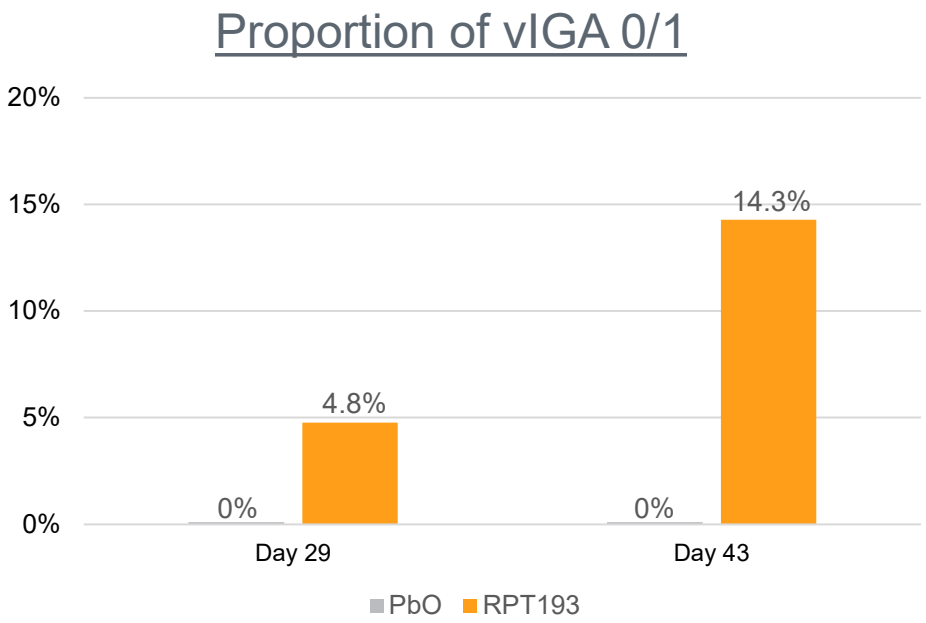
*p<0.05 (post-hoc analysis)

RPT193: EASI-75 and EASI-90

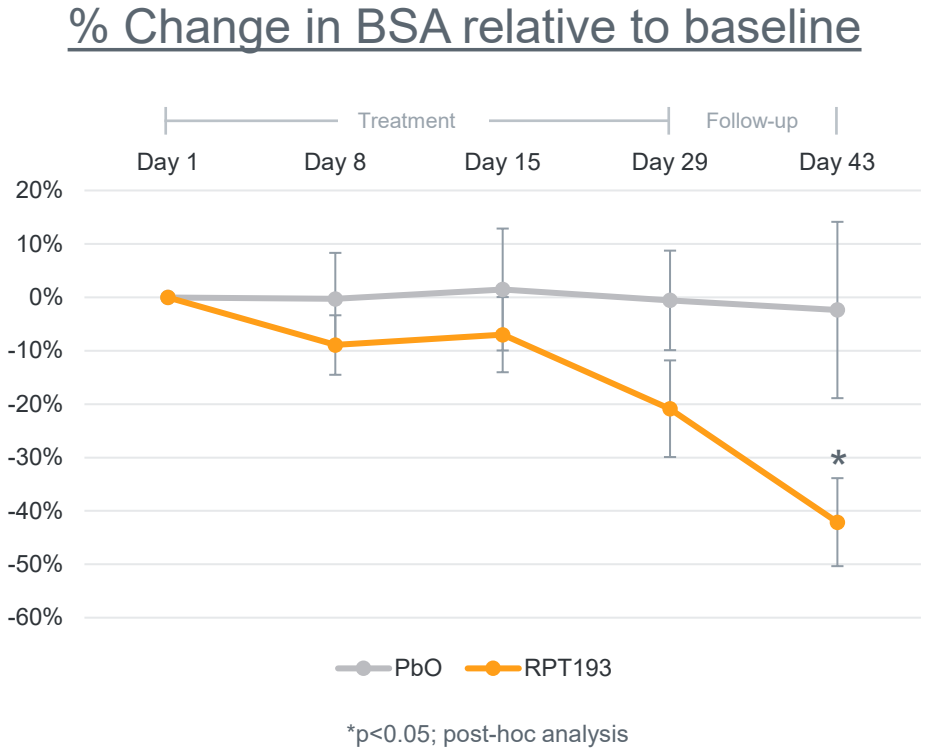




RPT193: vIGA 0/1 (Clear/Almost Clear at Day 29 and Day 43)



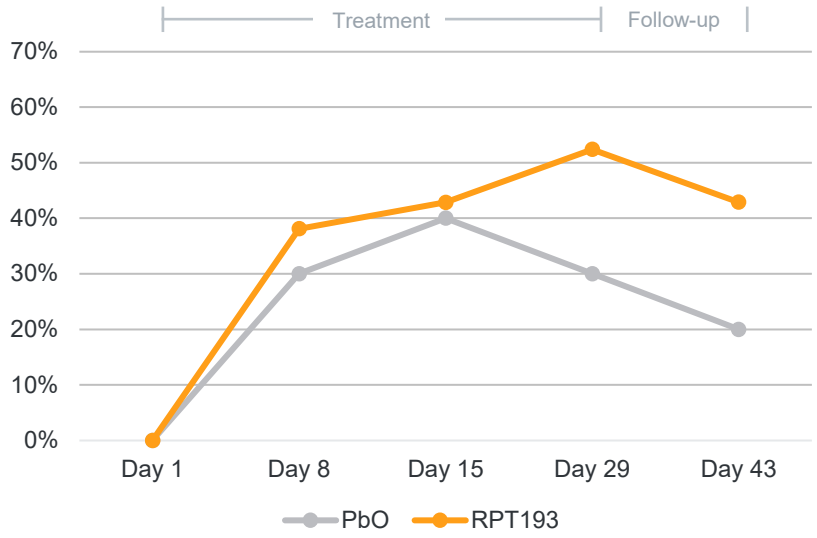
RPT193: Change from Baseline in BSA



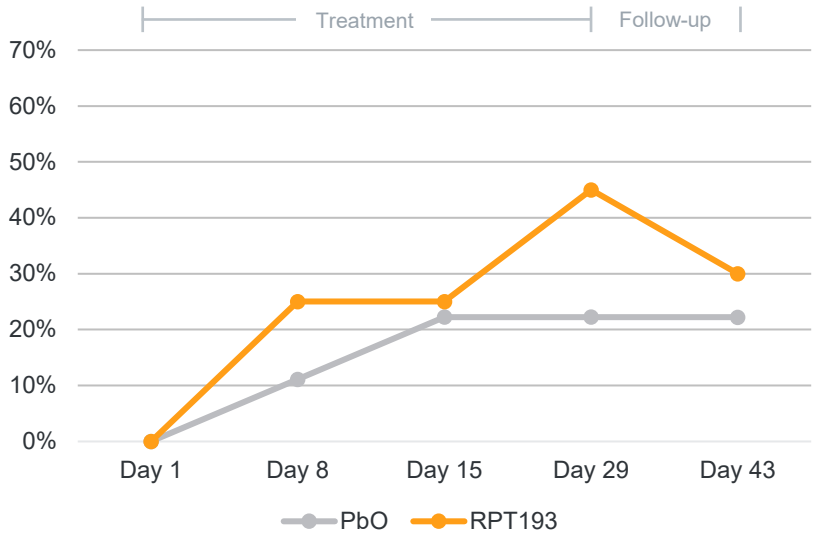
*p<0.05; post-hoc analysis

RPT193: Pruritus NRS: 3- or 4- Point Decrease from Baseline

Proportion of Subjects* with NRS 3-pt Drop



Proportion of Subjects** with NRS 4-pt Drop



*Among patients with a baseline PNRS of 3 or more
**Among patients with a baseline PNRS of 4 or more

Conclusions

- This is the first study conducted with a chemokine receptor antagonist that showed a positive efficacy signal in patients with AD
- CCR4 inhibition with once-daily, oral RPT193 was generally well tolerated after 28 days of dosing
- At the End of Treatment (Day 29), RPT193 showed improvement in EASI, EASI-50 and proportion of patients achieving a 4-pt drop in pruritus NRS
- At the End of Study (Day 43), RPT193 showed further improvement compared to Day 29 and placebo-treated patients
  - Improvement in EASI, EASI-50, BSA at Day 43 demonstrated statistical significance in a post-hoc analysis
- Further improvement after cessation of dosing could be consistent with unique kinetics associated with targeting Th2 cell migration and activation through CCR4 inhibition
- RPT193 has the potential to become a novel, oral treatment for patients with AD
- A dose-ranging Phase 2b trial is planned to further investigate RPT193's efficacy and safety in patients with AD

Acknowledgments

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