RAPT THERAPEUTICS

# Development and first-in-human characterization of a potent oral CCR4 antagonist for the treatment of atopic dermatitis

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**Plenary II**

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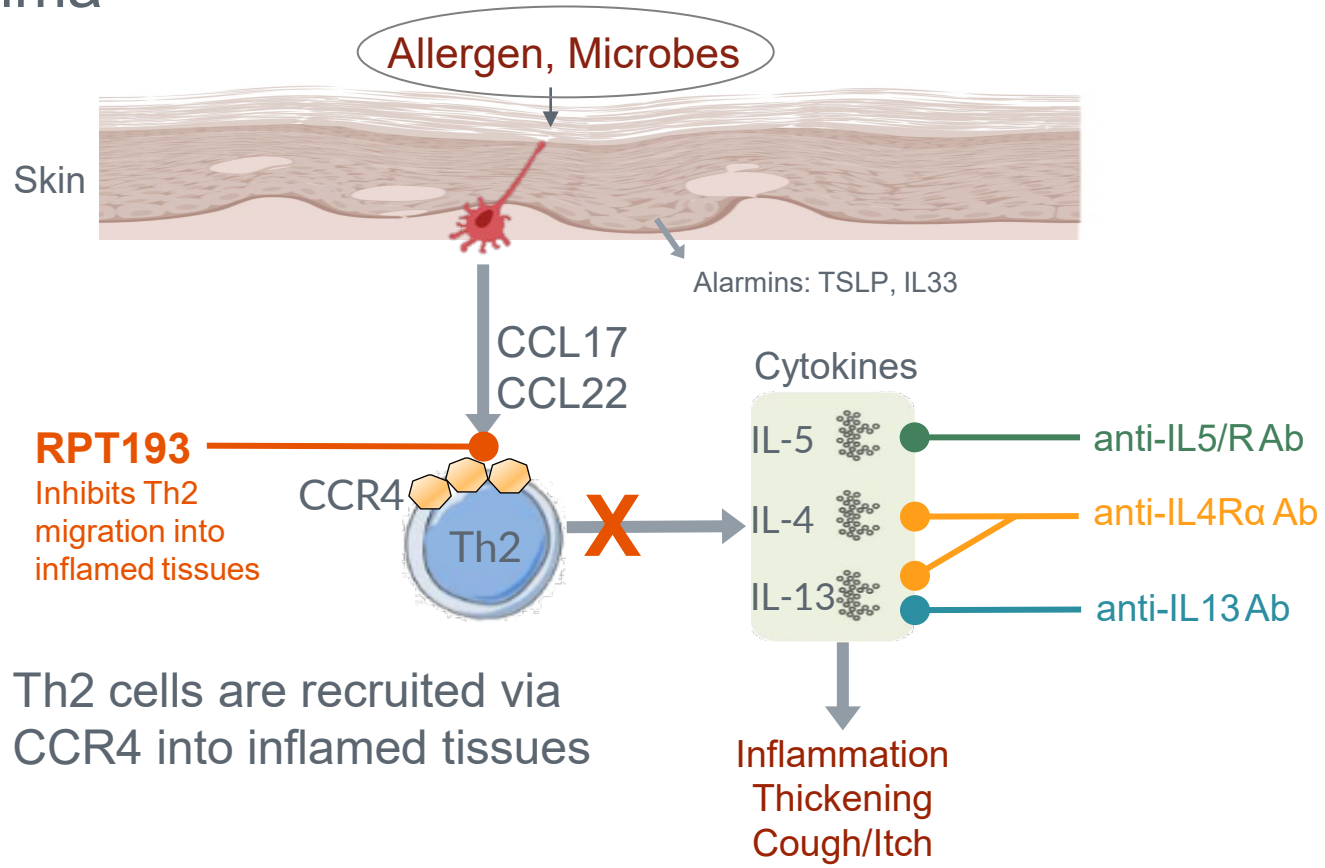
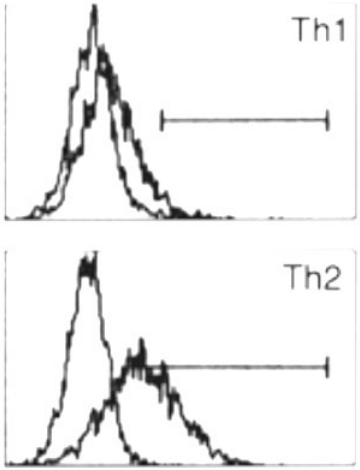
# Disclosures

- Laurence Cheng is a Current Employee and Shareholder of RAPT Therapeutics, Inc.

# RPT193 Acts on a Well Validated Pathway in Atopic Dermatitis and Asthma

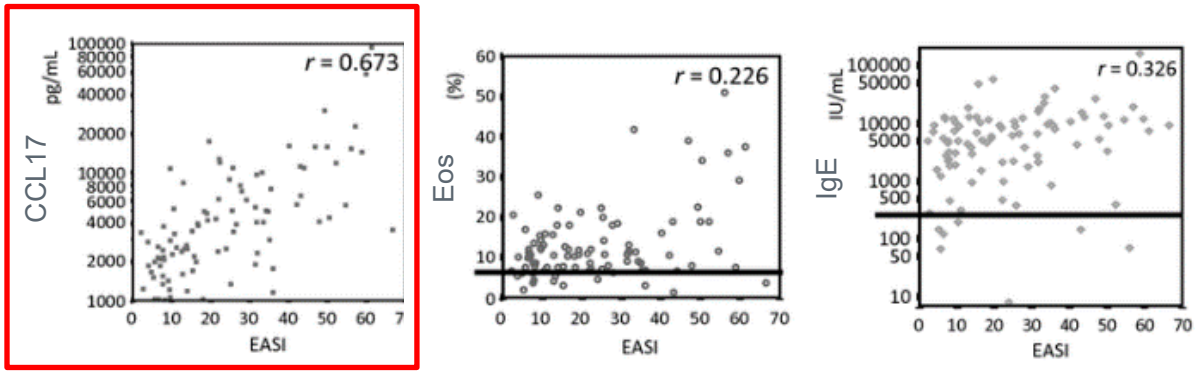


# CCR4 is Highly Expressed on Th2 cells and Elevated Levels of CCR4 Ligands Correlate with Disease Activity and Severity




**CCR4**

CCR4 is predominantly expressed on Th2 over Th1 Cells

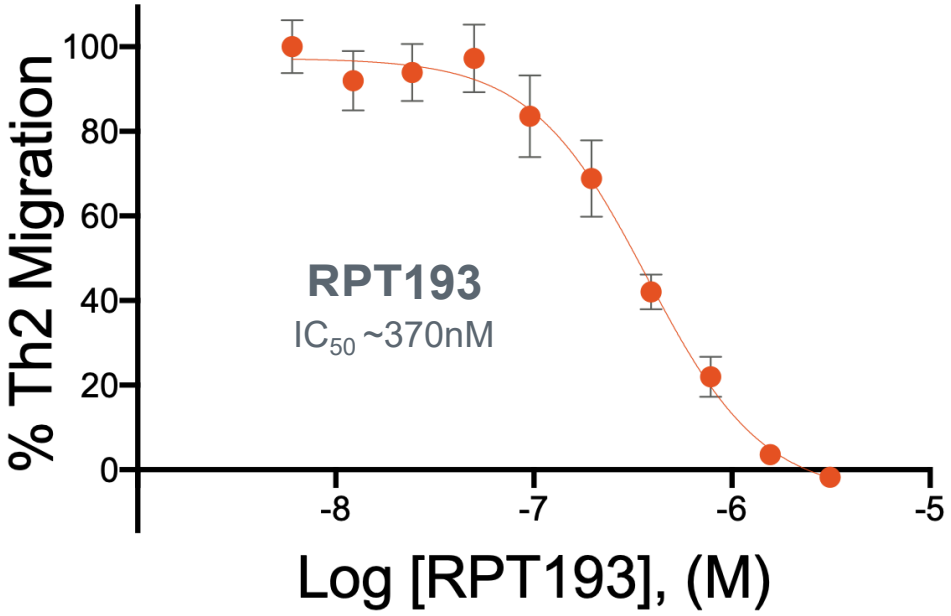


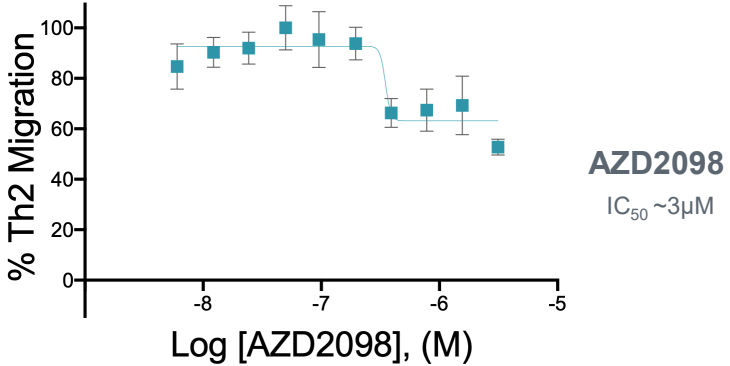

Serum CCL17 levels correlate more strongly with atopic dermatitis clinical activity and severity compared to other biomarkers

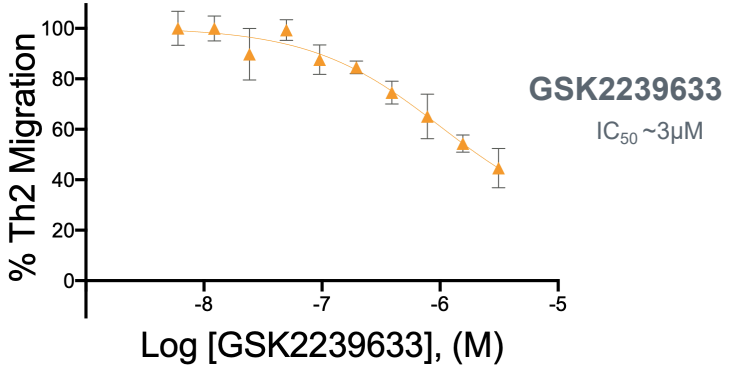
Imai et al. (1999 ) Int. Immunol., Kataoka et. al. (2014) *Journal of Dermatology*

# RPT193 Has Greater Potency Against Th2 Chemotaxis Than Previous CCR4 Antagonists

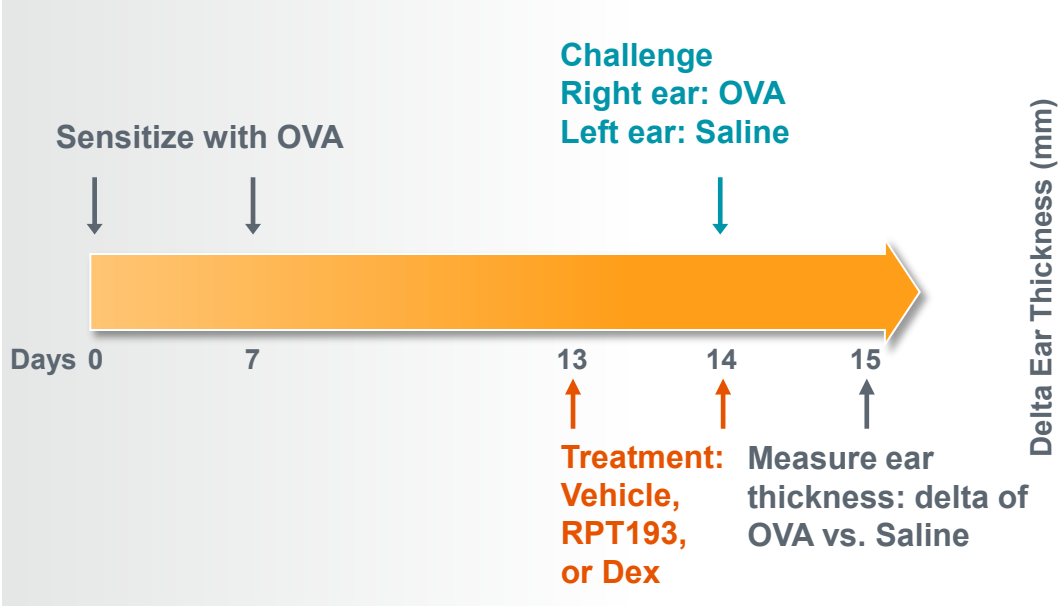
## CCL22-Induced Human Th2 Chemotaxis

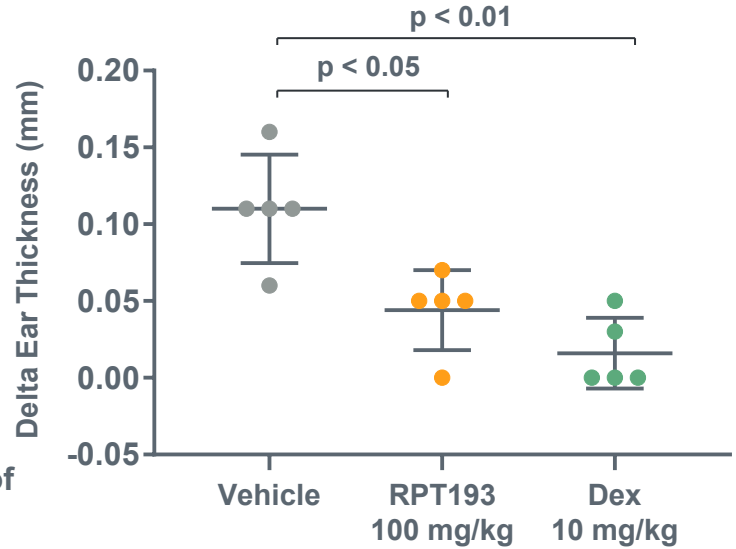


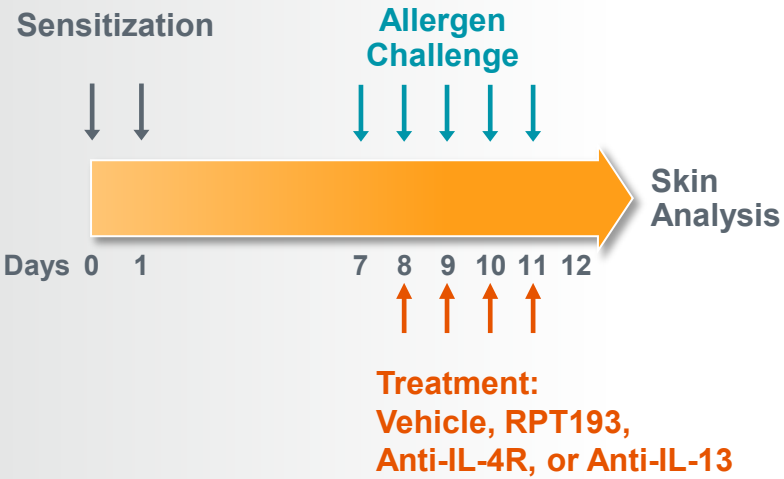
# Oral Doses of RPT193 Reduces Skin Inflammation in an Acute OVA-Induced Atopic Dermatitis Model

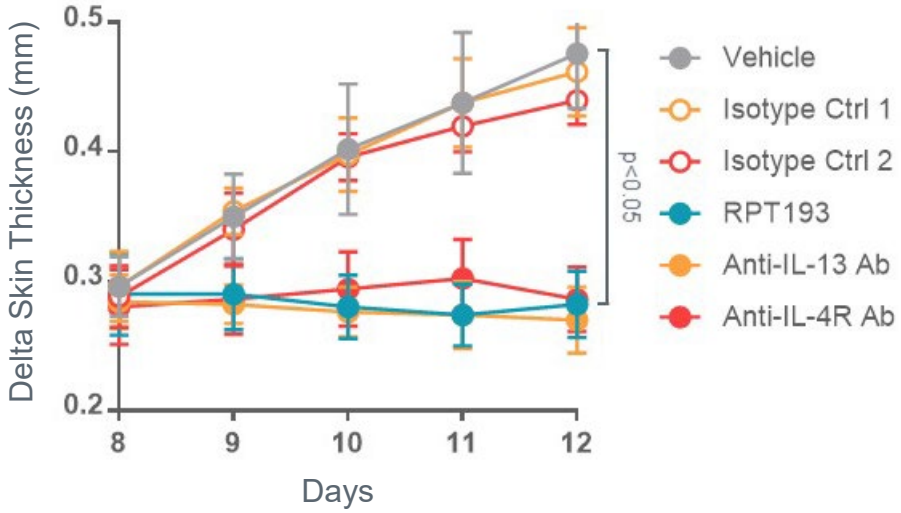


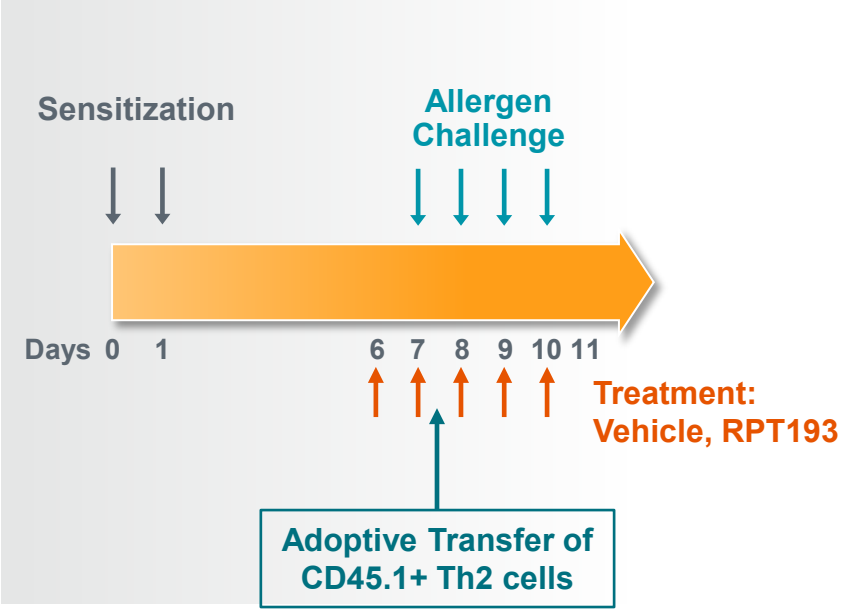

- 100 mg/kg QD oral dosing covers the mouse Th2 $IC_{90}$ for chemotaxis at trough

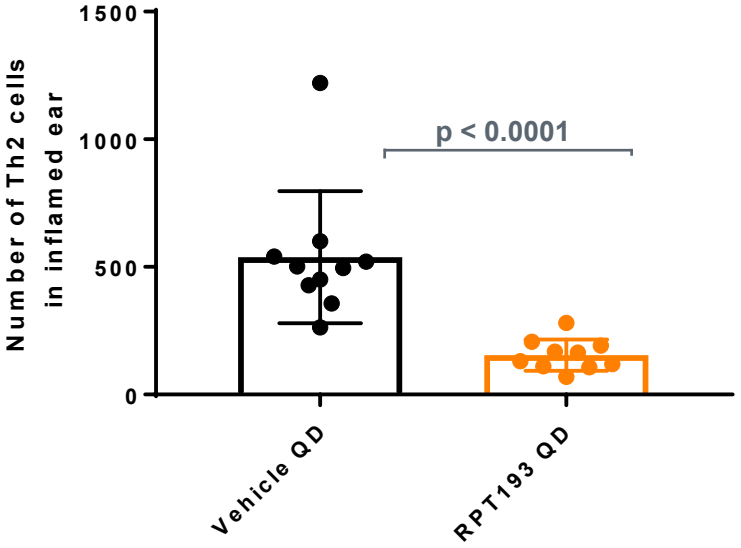
# Oral Doses of RPT193 Demonstrates Similar Efficacy to Biologics in a Therapeutic Atopic Dermatitis Model



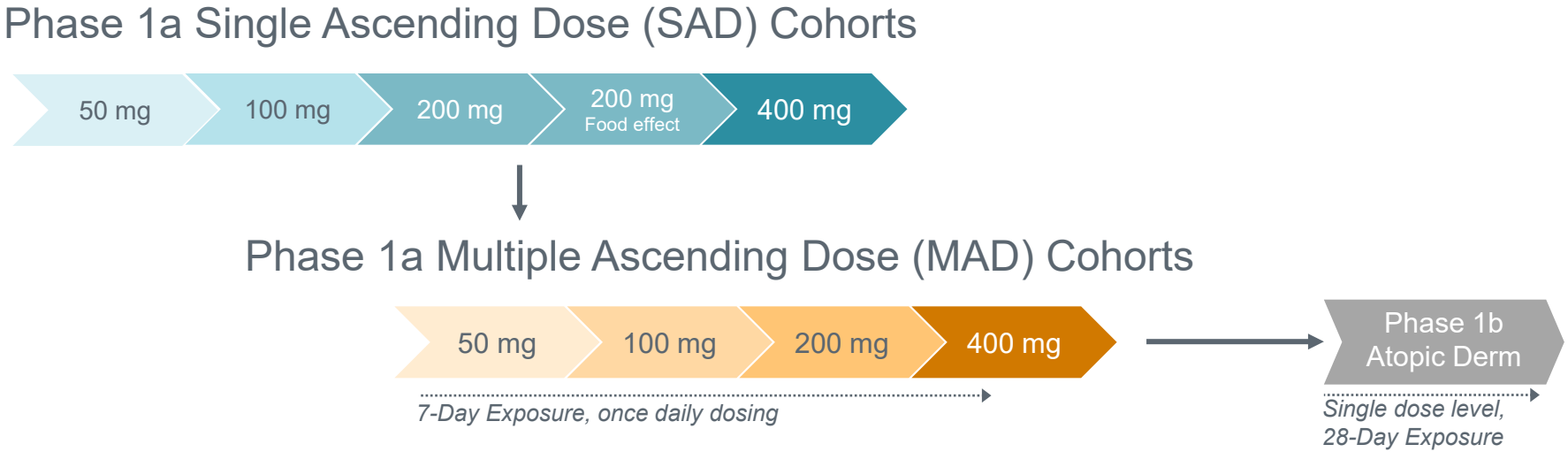



# RPT193 Significantly Reduces Th2 Cell Migration Into Inflamed Skin a Mouse AD Model



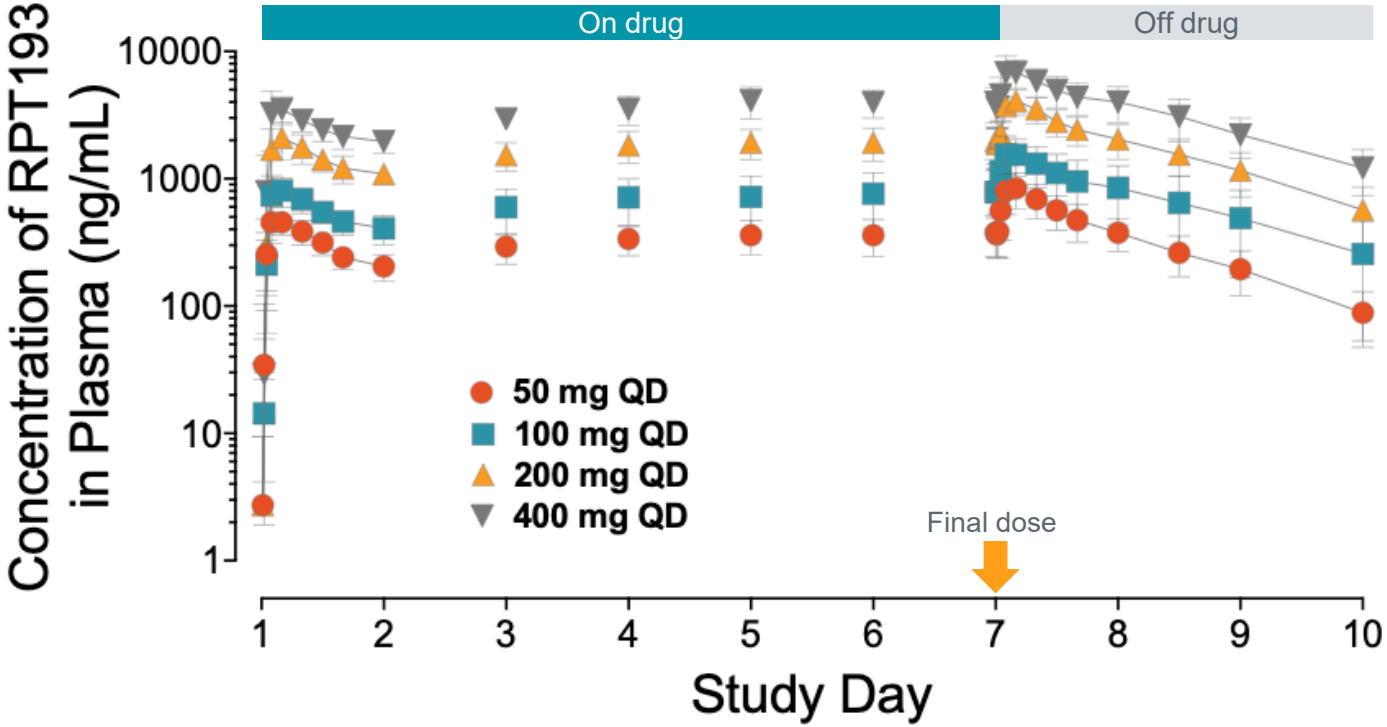
# RPT193: Seamless Phase 1 Starts in Healthy Volunteers and Includes an AD Patient Cohort to Establish Proof of Concept



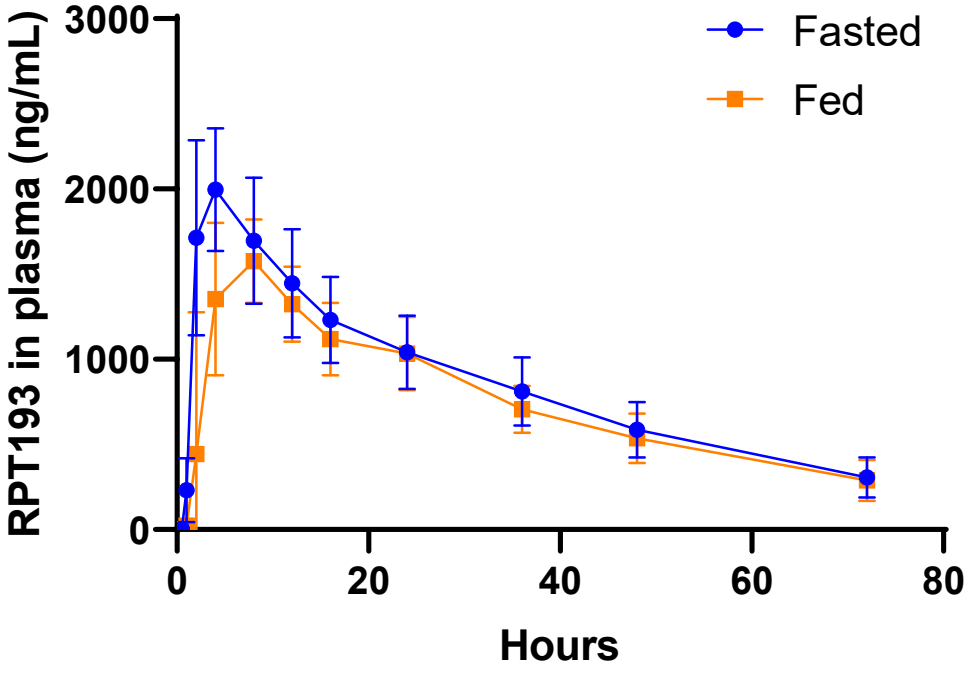

- Healthy Volunteer SAD and MAD Cohort Design
  - Double-blind, randomized study with 8 subjects per cohort (6 receiving oral RPT193 and 2 receiving placebo)
  - Effect of high-fat meal on pharmacokinetics tested after single 200 mg dose
  - Endpoints: PK, PD, Safety

# Phase 1a Healthy Volunteer Data Support Once-Daily Dose

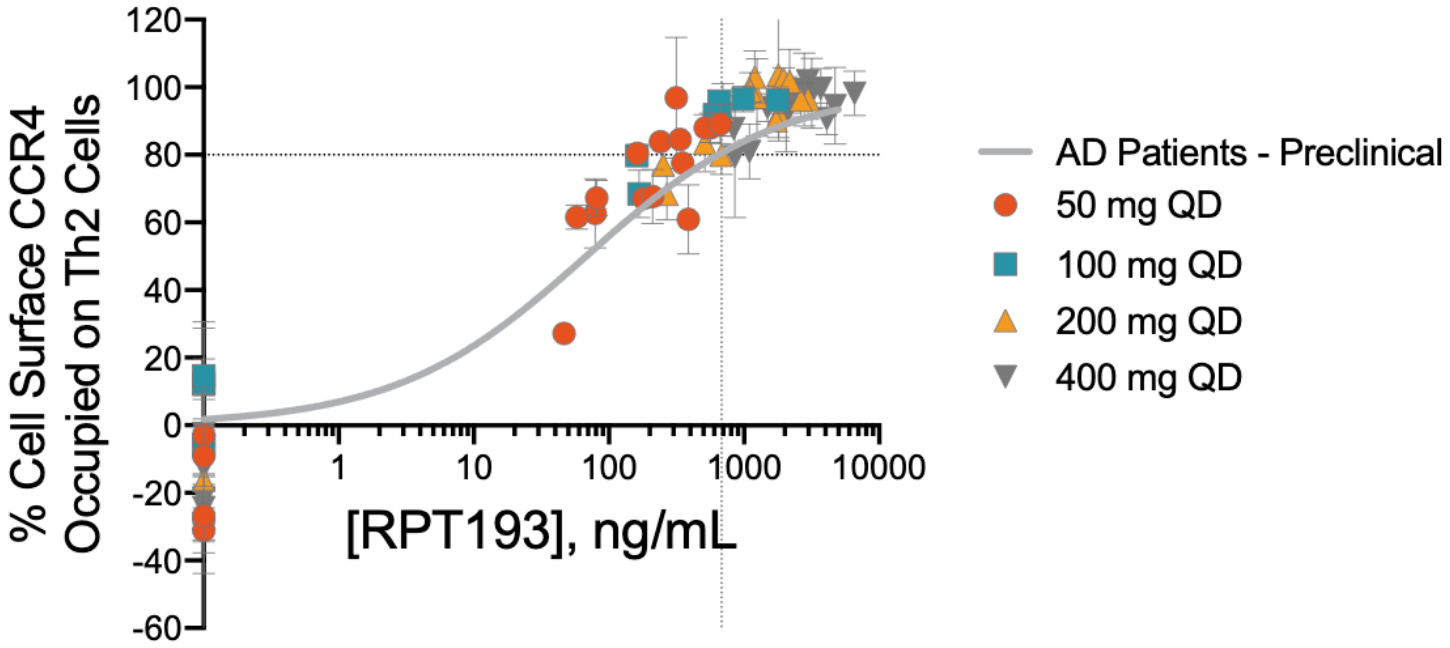
Dose-proportional Oral PK With Mean Terminal Half-life Of ~25 Hours Across All Dose Levels



# Minimal Effect of Food Observed on Pharmacokinetics of a Single 200 mg Oral Dose of RPT193



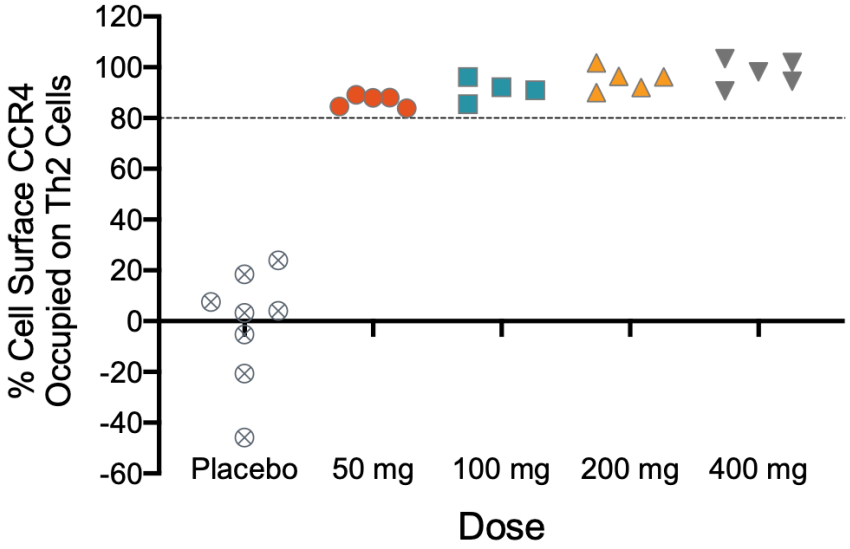
# RPT193 Exhibits Concentration-Dependent Target Occupancy Predicted to Inhibit CCR4-mediated Th2 Migration




Targeting 90% inhibition of Th2 chemotaxis

# Targeted CCR4 Inhibition is Achieved with Repeated 50 mg Daily Dosing

Inhibition at day 8 across the dose levels



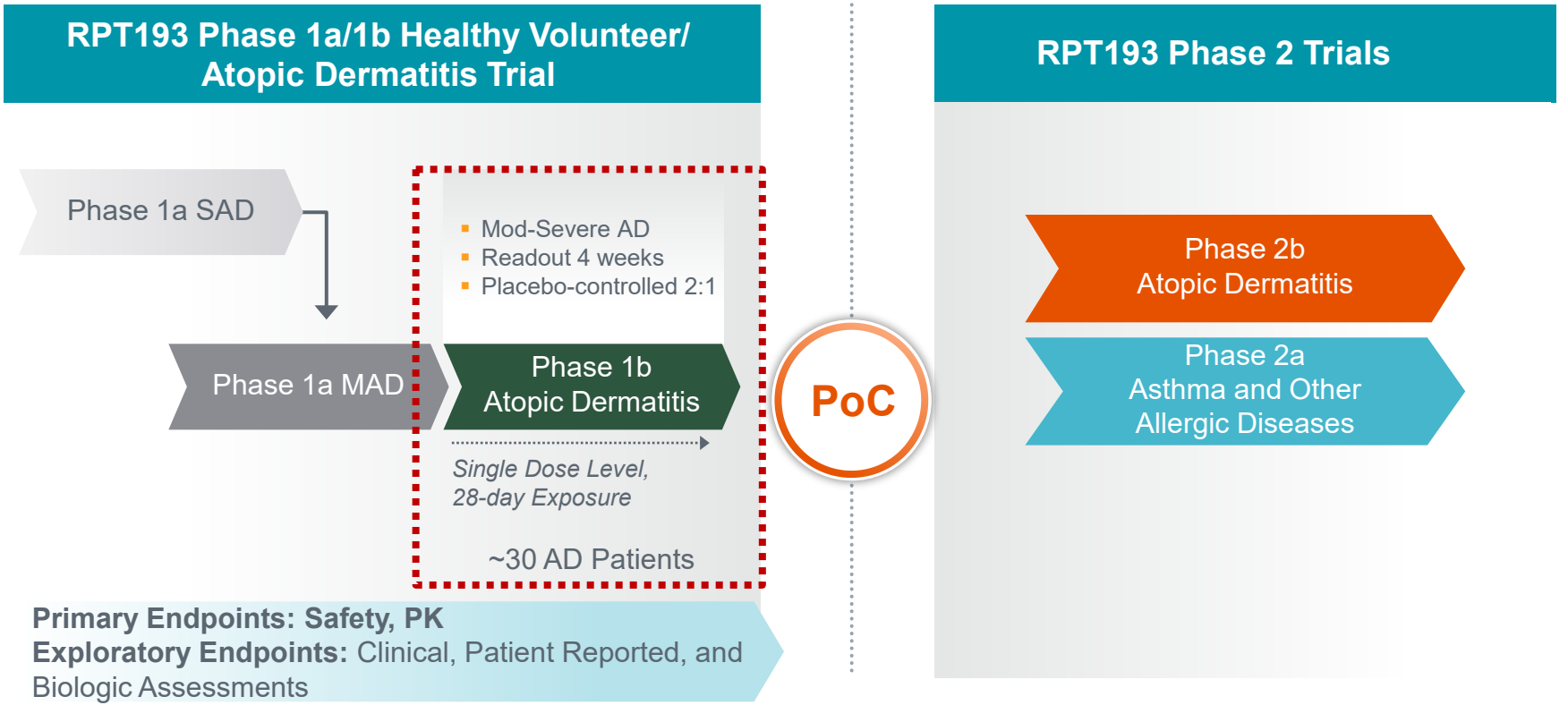

6 dosed / 2 placebo subjects per cohort
Analysis for some subjects did not pass QC, resulting in fewer than 8 points per cohort

# *Blinded* Safety Data Indicate RPT193 has been Well Tolerated

## SAD/MAD Safety Summary

- For the SAD and MAD, 64 subjects in total have been dosed with RPT193 or Placebo
- No Serious Adverse Events (SAEs)
- All (n=87) but one TEAE were mild in nature (single count of moderate headache in the MAD)
- No apparent increase in intensity or number in a dose-related fashion
- No ECG or lab related findings of note, including hematologic indices

# RPT193: Seamless Clinical Trial Design to PoC and Beyond



# RPT193 has Demonstrated Promising Preclinical Efficacy and Early Clinical Data in Healthy Volunteers

- Therapeutic effects comparable to anti-IL4R alpha and anti-IL13 in mouse models of allergic skin inflammation
  - RPT193 blocks Th2 migration via targeting of CCR4
- Clean safety profile and well tolerated after single dose and multiple doses for 7 days of 50-400 mg in healthy volunteers
  - In addition, RPT193 GLP toxicology studies show a safety profile favorable for chronic, allergic disease indications
- Pharmacokinetics data support once daily oral dosing
  - Dose proportional exposure with low intra-subject variability
  - Minimal food effect
- Achieved target CCR4 inhibition in 100% of subjects at multiple doses of 50 mg and above
- A Phase 1b randomized, double-blind, placebo-controlled cohort enrolling moderate to severe AD patients is ongoing

# Acknowledgements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