



Transforming the Treatment of Cancer and Inflammation

April 2022
Corporate Presentation

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Oral Drugs Targeting Critical Immune Drivers of Disease

- Proprietary discovery engine
- Diversified pipeline
- Large market opportunities
- Clinically de-risked assets
- Strategic collaborations

CLINICAL

RPT193 (Inflammation):

- Oral agent targets inflammatory Th2 cells
- PoC in Phase 1b achieved in AD: efficacy on all key exploratory endpoints with excellent safety and tolerability

FLX475 (Oncology): MERCK

- Selectively targets immunosuppressive tumor T_{reg}
- PoC in Phase 2 with monotherapy and combo activity observed

DISCOVERY

HPK1 (Oncology)

Other Targets

Proprietary Drug Discovery and Development Engine

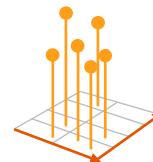
Rapid

- Drug discovery
- Clinical development to POC



Analytics

- Interrogating clinically-relevant big datasets to identify targets and biomarkers



Patient selection

- Driven by data to improve chances of clinical success



Targeting

- Critical immune drivers of cancer and inflammation



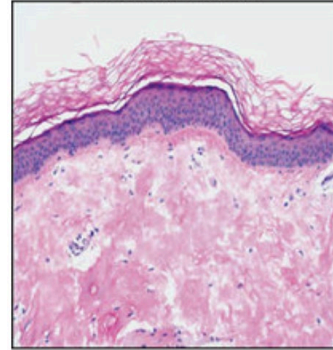


RPT193: CCR4 Antagonist for Inflammatory Diseases

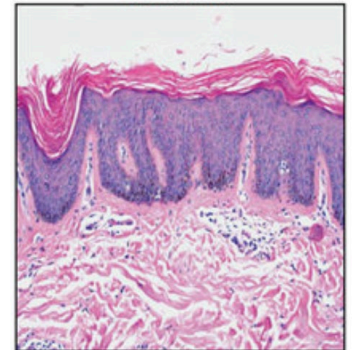
RPT193: Oral CCR4 Antagonist for Inflammatory Diseases

- RPT193 is a highly potent and selective once-daily oral CCR4 antagonist designed to safely reduce inflammation in a broad range of allergic disorders
- Phase 1b trial demonstrated clear benefit in patients with moderate-to-severe AD, with favorable safety and tolerability
- No laboratory safety monitoring or black box warning expected
- Next steps: Phase 2b trial in AD and a Phase 2a trial in asthma

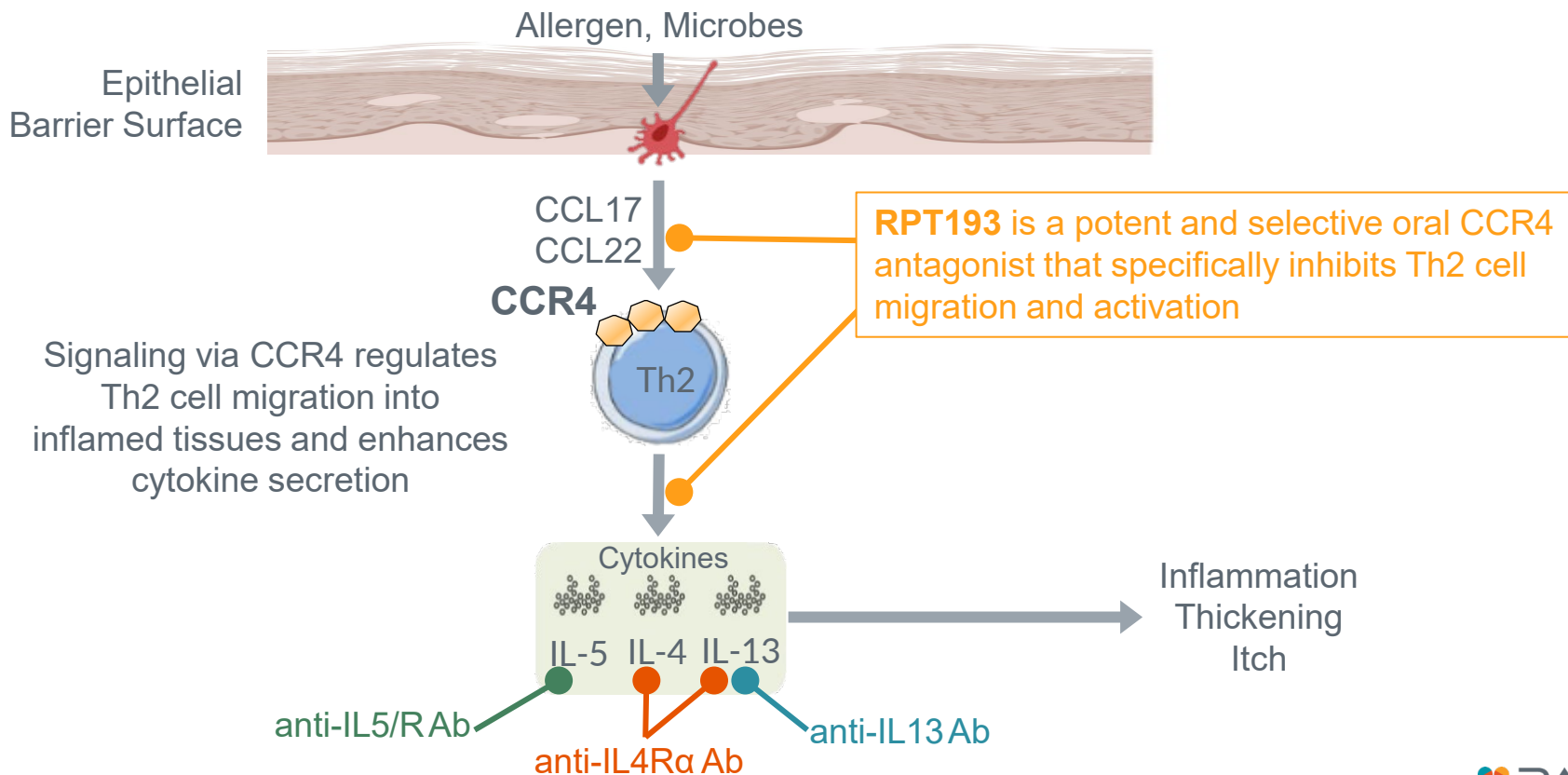
Normal Human Skin



AD Lesional Skin



RPT193 Targets Th2 Cells: Key Drivers of Inflammation in Atopic Dermatitis, Asthma, and Other Diseases



Atopic Dermatitis and Asthma Represent Major Markets

- **Atopic Dermatitis (AD)**

- Common disease affecting ~19M adults and ~10M children in the US
- \$24B projected market by 2029*

- **Asthma**

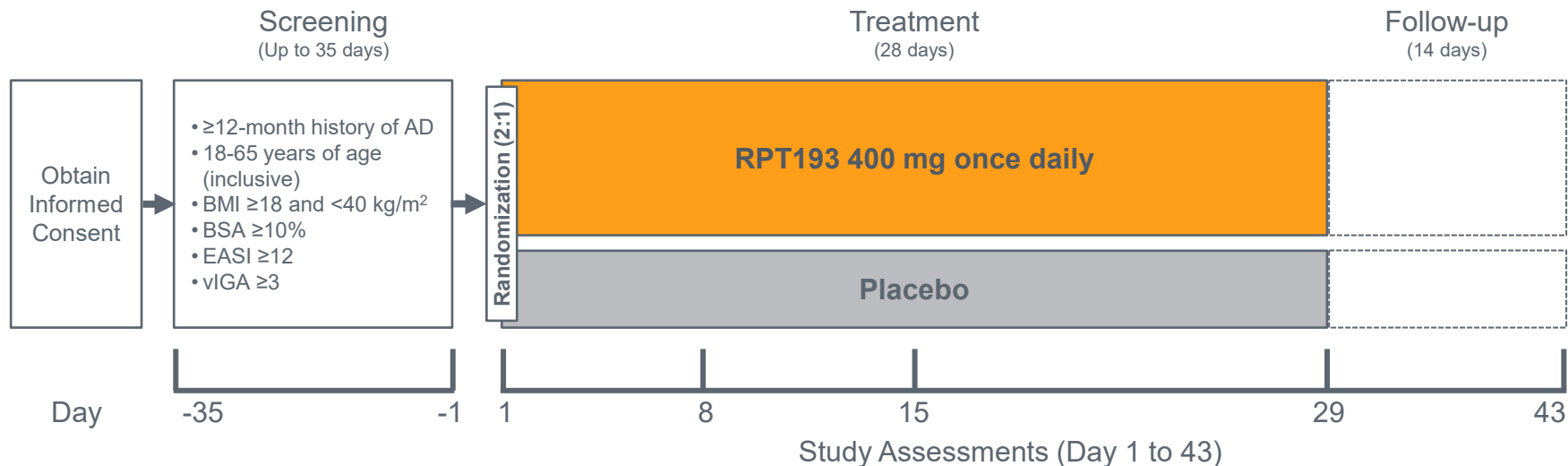
- Asthma affects ~15M adults and children in the US
- \$21B projected market by 2029*

- **High unmet need:** a well-tolerated, safe and effective, oral drug that does not require laboratory safety monitoring

- **RPT193 has the potential to address this unmet need**

* Decision Resources Guide; EU, US, and Japan market

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



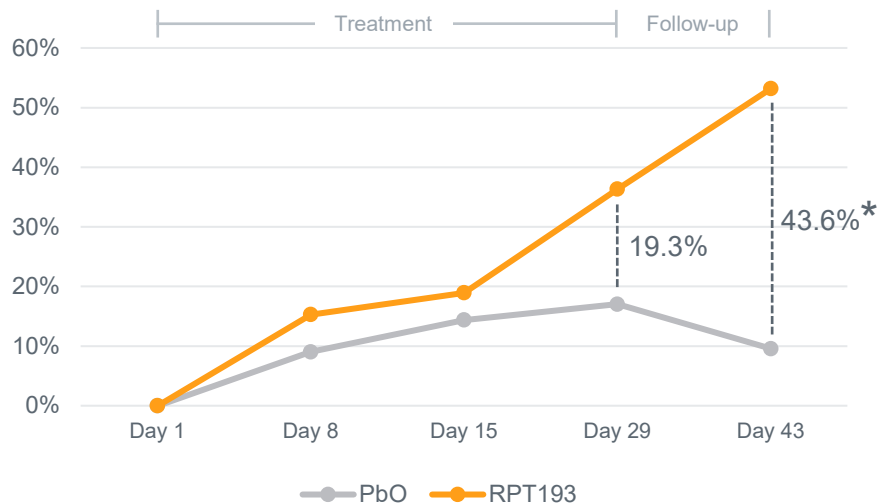
- Enrolled 31 patients into a double-blind, randomized trial with 2:1 allocation of RPT193 to placebo
- Monotherapy study: steroid and immunosuppressant washout period; rescue steroids not permitted through Day 43
- Trial was not powered for any specific endpoint
- Exploratory endpoints include: EASI, Pruritus Numerical Rating Scale (NRS), SCORAD, and vIGA
- Data presented are from the Intent to Treat dataset

Phase 1b Baseline Demographics and Disease Characteristics

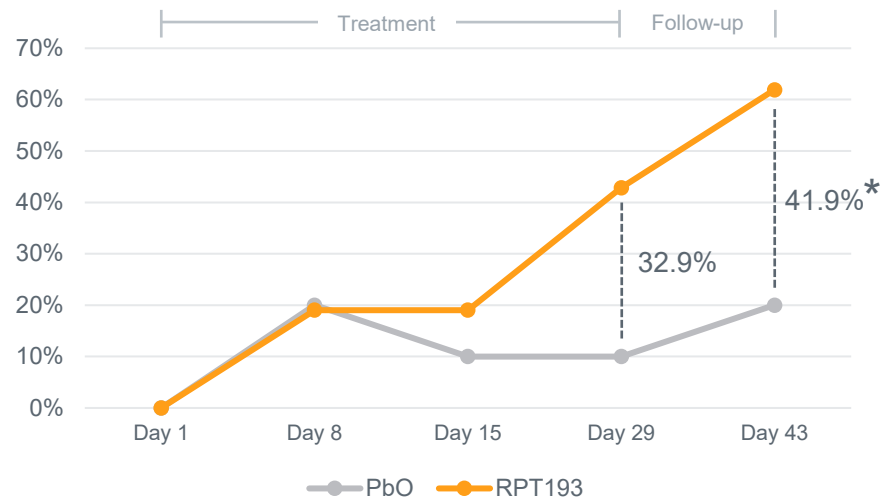
	Placebo	RPT193
N	10	21
Age, Mean (Range)	35.8 (22-64)	41.0 (19-63)
Female, n (%)	4 (40.0%)	12 (57.1%)
Baseline Characteristics		
EASI, Mean (Range)	21.07 (13.6-45.5)	18.49 (12-30)
BSA, Mean (Range)	24.5 (10-61)	23.3 (11-55)
vIGA 3, n (%)	8 (80.0%)	18 (85.7%)
Peak NRS, Mean (Range)	7.3 (3-10)	6.9 (3-10)
Peak NRS \geq 4, n (%)	9 (90.0%)	20 (95.2%)

RPT193 Differentiated from Placebo for EASI and EASI-50 at Day 29 with Further Improvement at Day 43

% Improvement in EASI



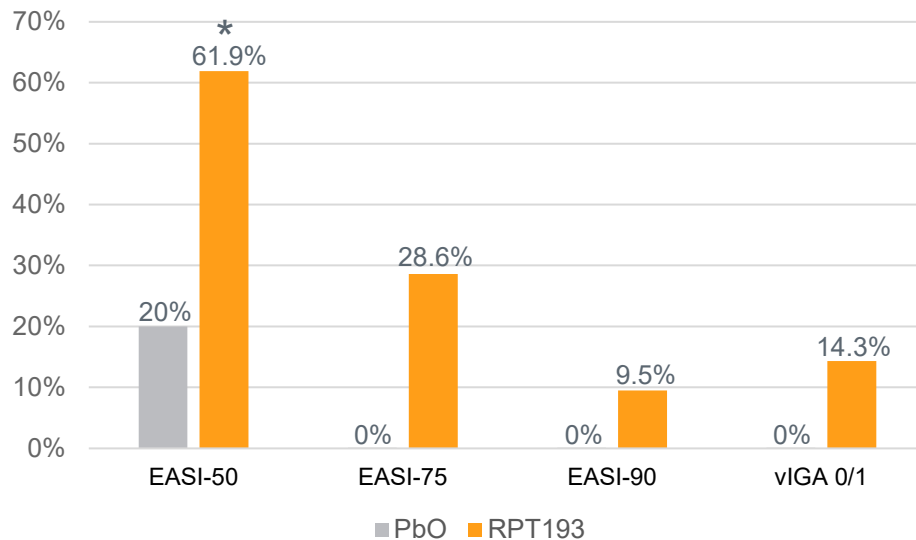
Proportion of EASI-50



*p < 0.05

RPT193 Differentiated from Placebo on EASI-75, 90 and vIGA 0/1 at Day 43

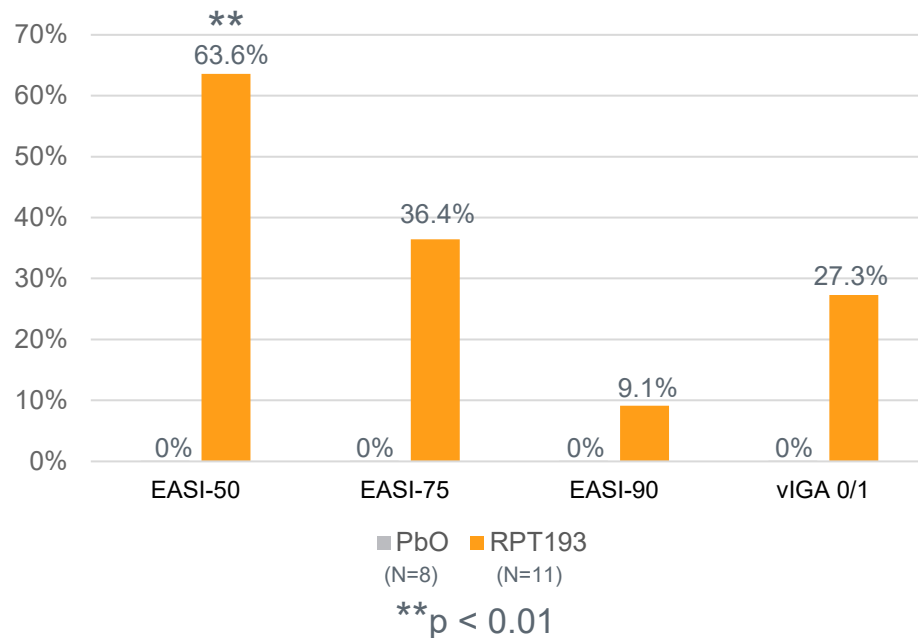
Proportion of EASI-50, 75, 90 and vIGA 0/1 (Clear/Almost Clear)



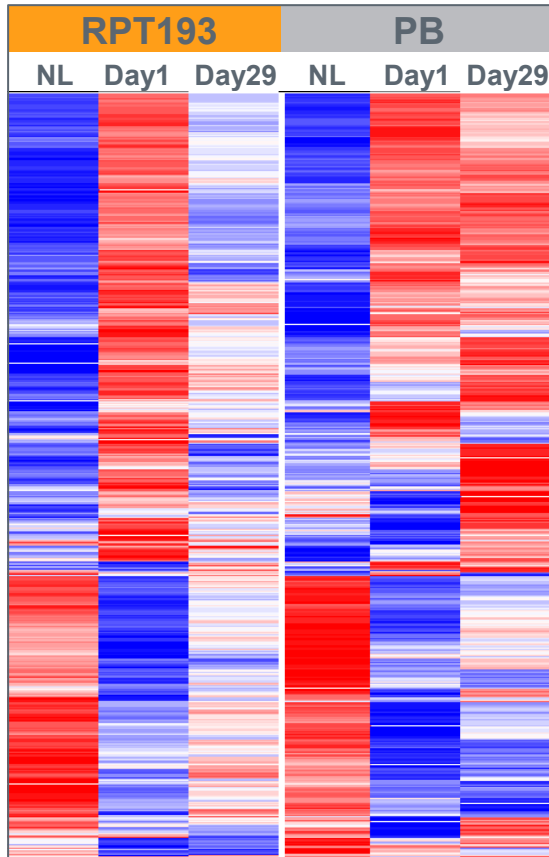
*p < 0.05

RPT193 Differentiated from Placebo on EASI-75, 90 and vIGA 0/1 at Day 43 in Patients with Baseline EASI \geq 16

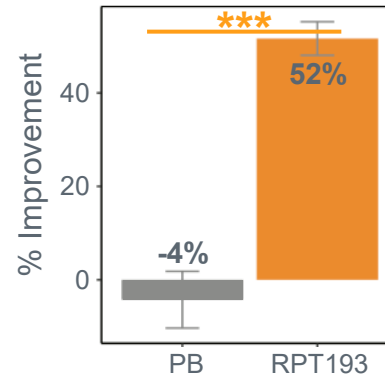
Proportion of EASI-50, 75, 90 and vIGA 0/1 (Clear/Almost Clear)



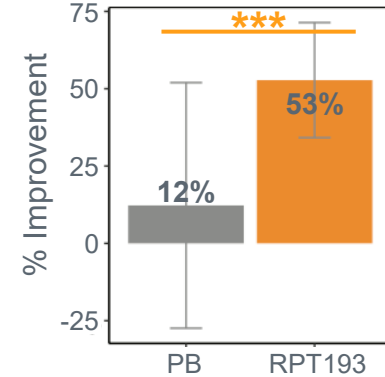
RPT193 Demonstrated Significant Improvement in AD-Associated Gene Signatures in the Skin



Mean % Improvement in MADAD Transcriptome



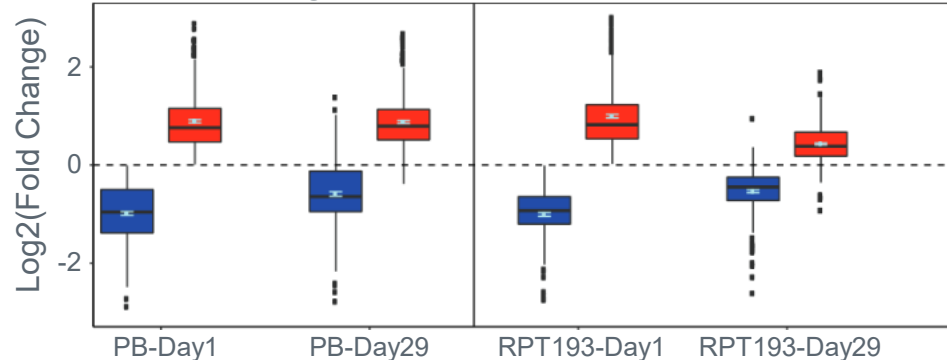
Median % Improvement in MADAD Transcriptome



*** (p < 0.001)

MADAD: Meta-Analysis Derived AtopiC DermatitiS score

Changes in the Lesional AD Transcriptome

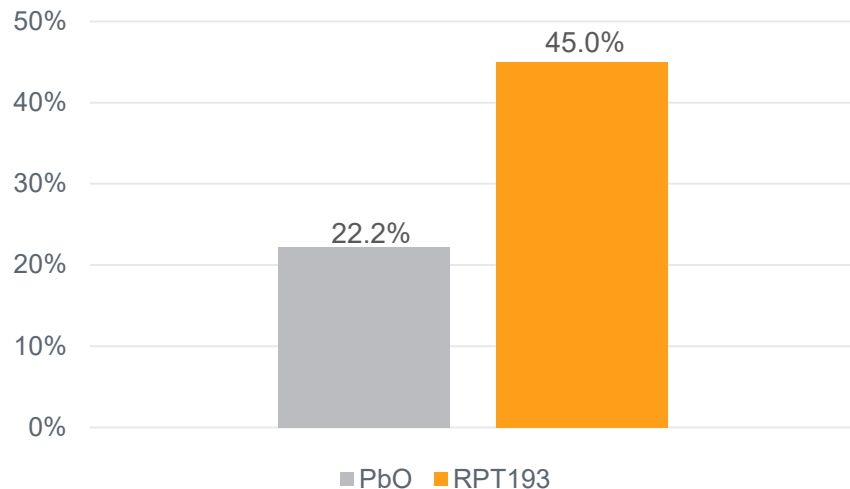


Direction of Dysregulation in AD:

■ Up-Regulated
■ Down-Regulated

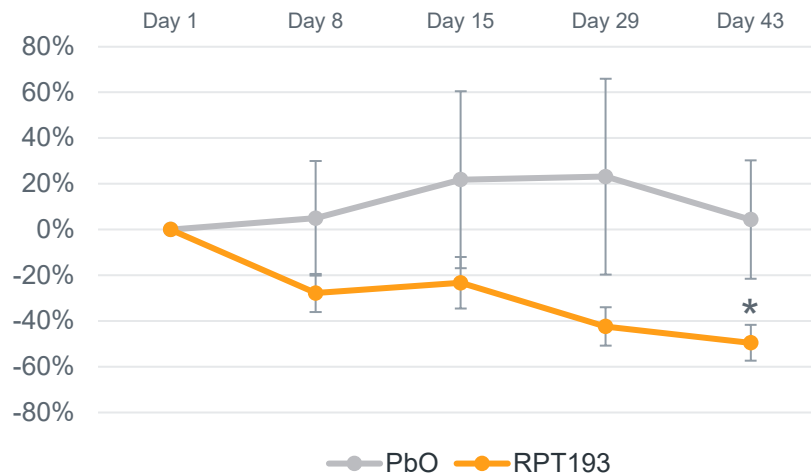
RPT193 Demonstrated Improvement in Itch and Sleep

Proportion of NRS-4[†]



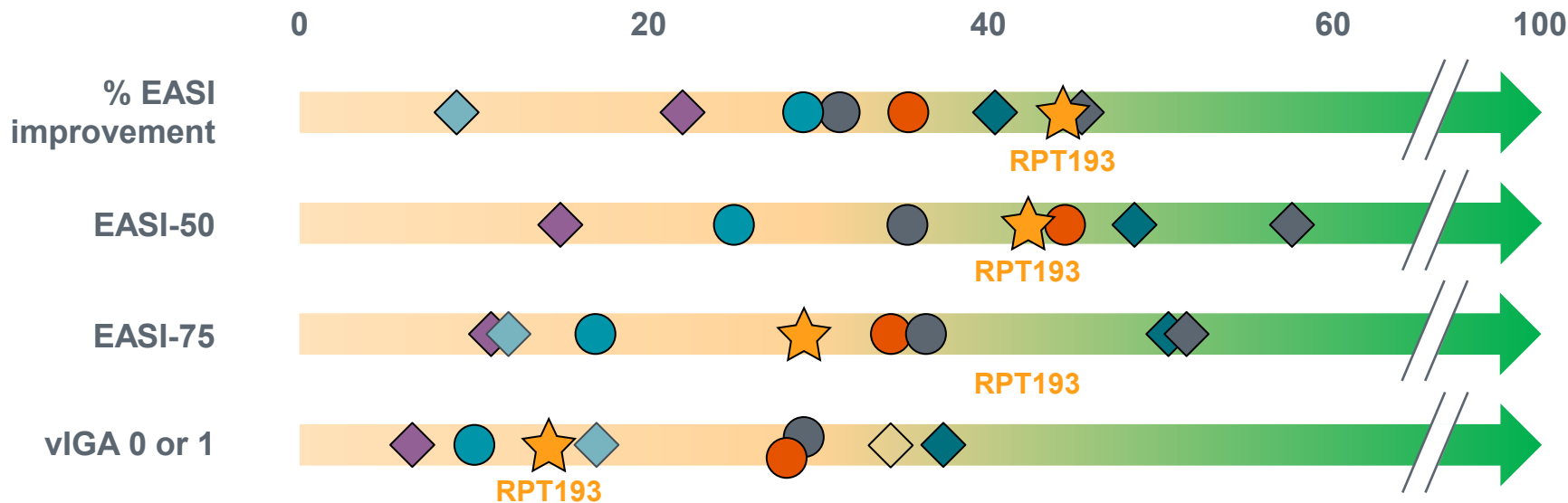
[†]At least a 4-point improvement among patients with a baseline pruritus NRS ≥ 4

% Change in Subjective SCORAD (Sleep Loss + Pruritus)



*p < 0.05

RPT193 6-Week Efficacy Compared to Other Drugs at 12-16 Weeks*



All data shown are placebo-adjusted

★ RPT193
400 mg

● Dupilumab Ph3 (300 mg q2wk)
● Lebrikizumab Ph2 (250 mg q2wk)
● Tralokinumab Ph3 (300 mg q2wk)

◆ Abrocitinib Ph3 (200 mg)
◆ Baricitinib Ph3 (2 mg)
◆ Etrasimod Ph2 (2 mg)
◆ Upadacitinib Ph2,3 (15 mg)

Biologics

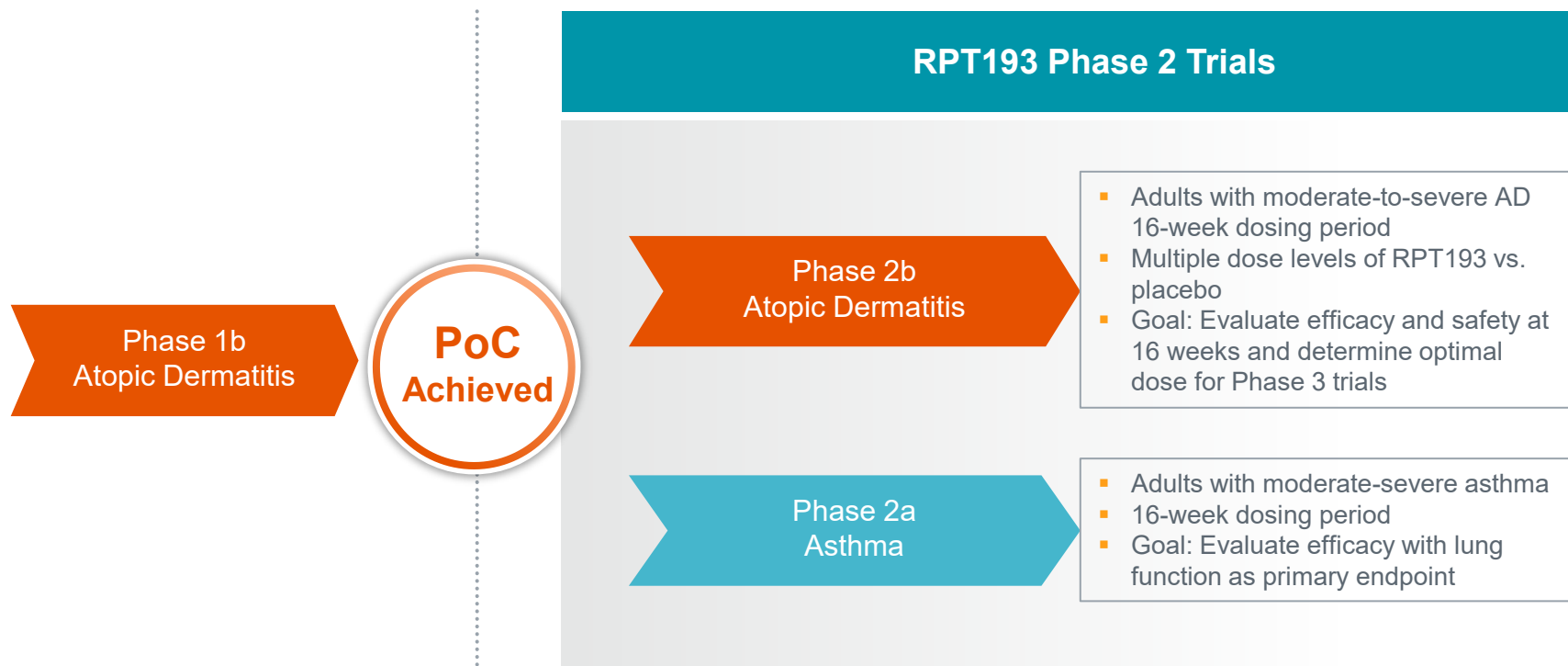
Orals

* Comparisons are based on published data and relative properties of other agents and do not reflect a head-to-head comparative study or clinical trial

Phase 1b Safety

- No SAEs reported
- All AEs reported were mild or moderate in intensity
- No clinically significant safety laboratory abnormalities observed
- Overall safety profile to date suggests a well-tolerated oral drug that should not require laboratory safety monitoring

Next Steps for the RPT193 Program



Potential “Pipeline in a Product”

Dermatology

- Atopic Dermatitis
- Chronic Urticaria
- Alopecia Areata
- Prurigo Nodularis
- Bullous Pemphigoid

Respiratory

- Asthma
- COPD (Th2 high)
- IPF

Allergy

- Chronic Rhinosinusitis
- Allergic Rhinitis
- Eosinophilic Esophagitis

Th2-Driven Inflammatory Diseases

RPT193 Program Summary

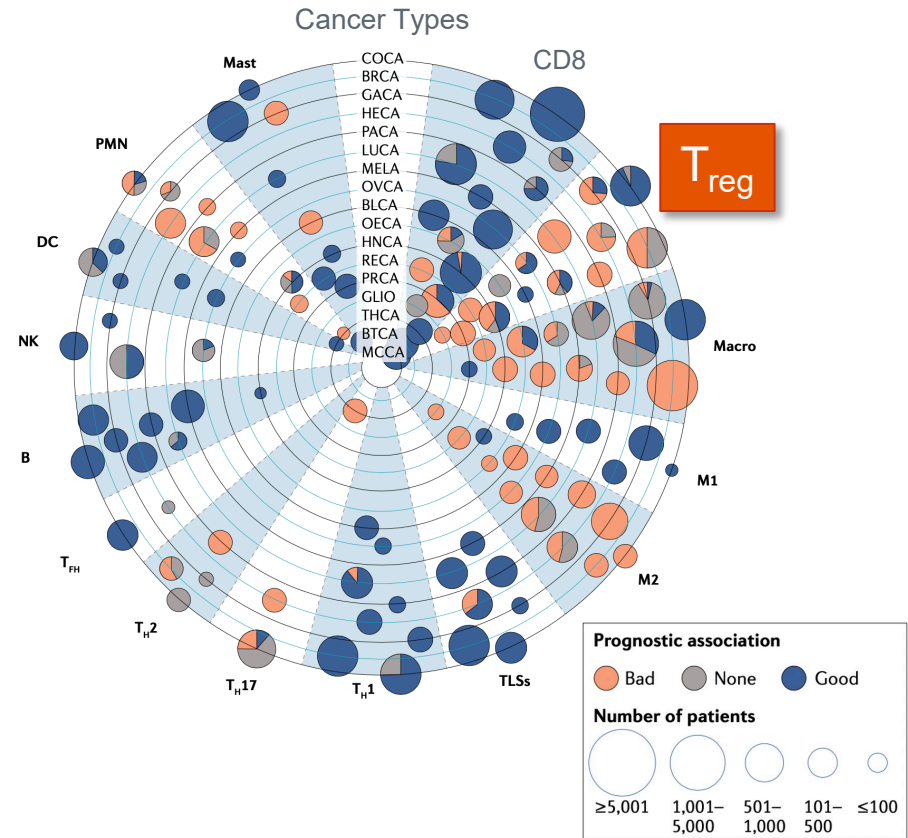
- Data from the Phase 1b study in patients with atopic dermatitis demonstrated clear benefit on all key exploratory clinical endpoints including EASI and vIGA
- Continued deepening of responses through the 2-week follow-up period suggests higher levels of efficacy could be achieved in longer studies
- Profile suggests an effective, well-tolerated oral molecule not needing laboratory safety monitoring, with positioning ahead of injectables and JAK inhibitors
- Next steps: 16-week Phase 2b study in patients with moderate-to-severe AD and a Phase 2a study in patients with asthma



FLX475: CCR4 Antagonist for Oncology

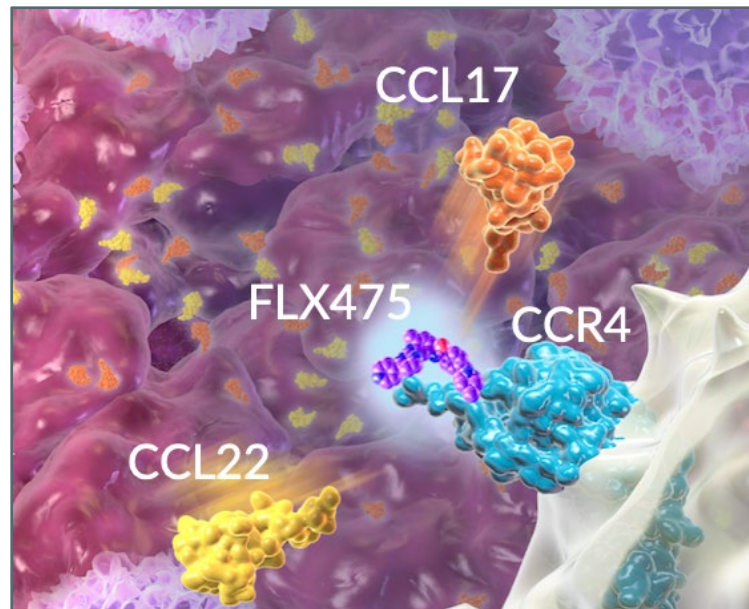
T_{reg} Are Key Targets in the Tumor Microenvironment (TME)

- Correlate with poor prognosis across most cancers
- Mechanism for immune evasion by viruses and tumors
- Barrier to checkpoint inhibitor efficacy
- Challenge: selective inhibition of T_{reg} in the TME
 - Depleting antibodies targeting CD25, CCR4, etc. do not appear to have adequate selectivity



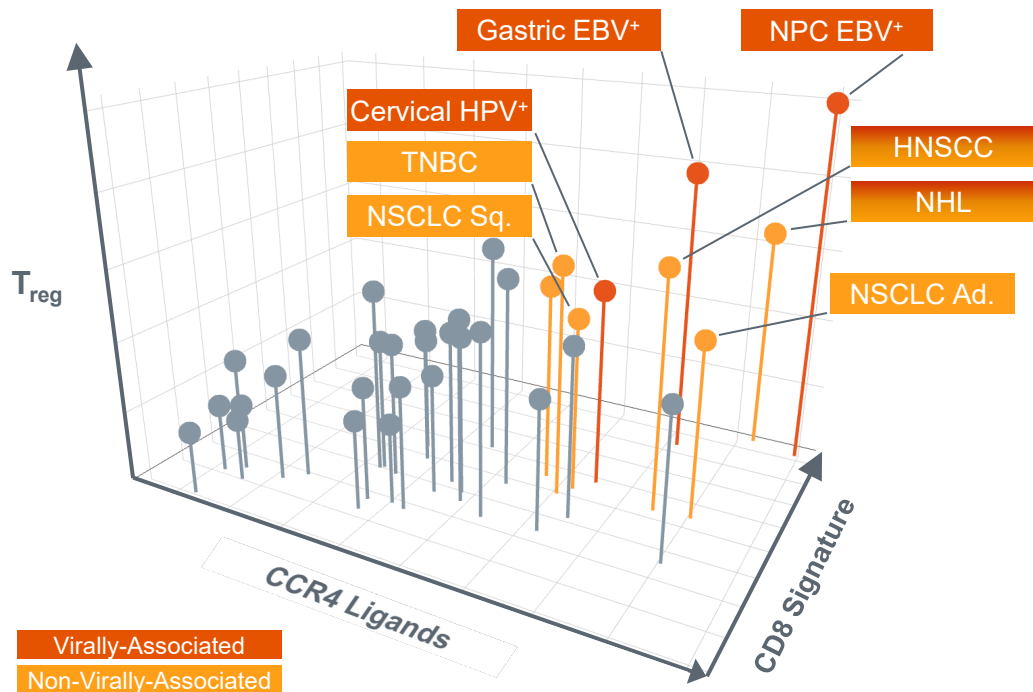
FLX475: Oral CCR4 Antagonist in Phase 2

- Highly potent and selective CCR4 small molecule antagonist
- Selectively blocks tumor T_{reg} while sparing normal tissues and beneficial cells
- Potential for superior safety and efficacy compared to depleting antibodies
- Issued U.S. composition of matter patent with coverage through 2037
- Monotherapy and combination antitumor activity in charged cancers



Blocks interaction with CCR4 ligands
CCL22 and CCL17 on T_{reg}

Identification and Characterization of Charged Tumors

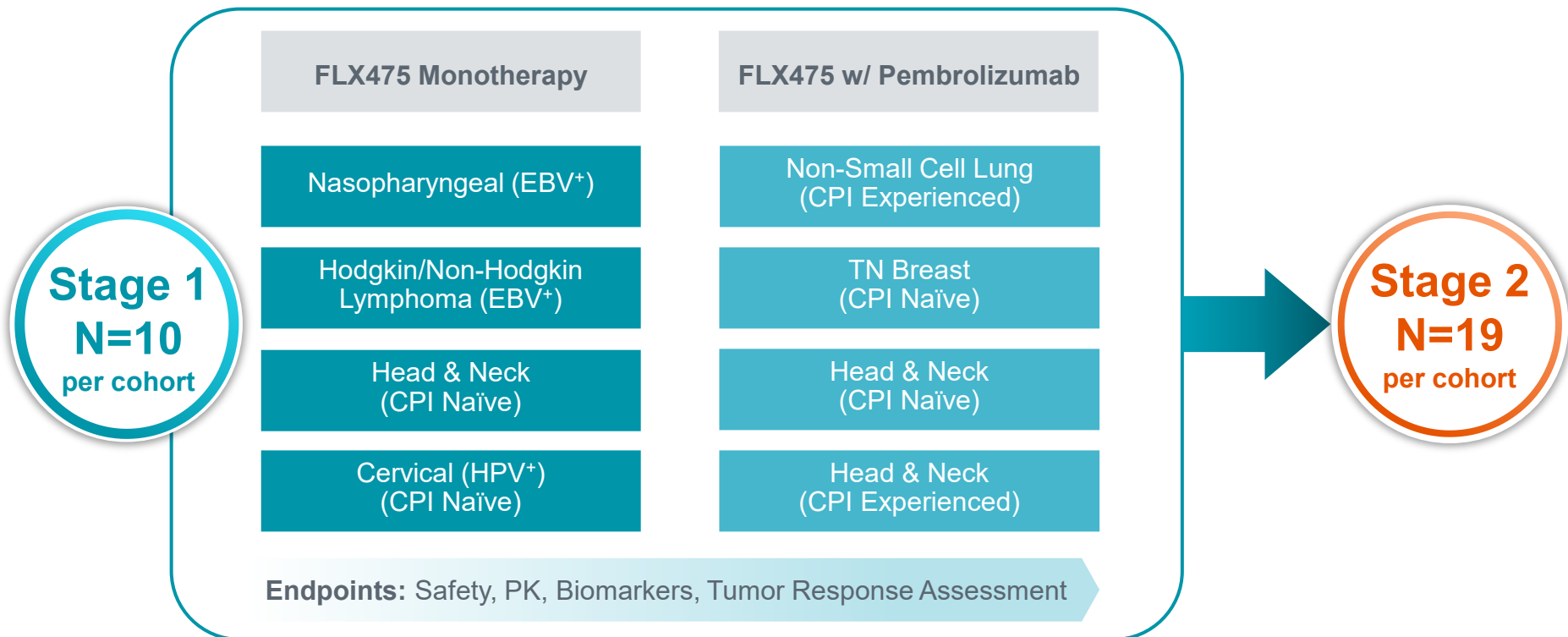


Data from in-house analysis of TCGA database combined with other data sets;
Confirmed in > 400 tumor microarrays
The graph above reflects a logarithmic scale on each axis
NPC Nasopharyngeal; HNSCC Head & Neck Squamous Cell Carcinoma; NHL Non-Hodgkin
Lymphoma; NSCLC Non-Small Cell Lung Cancer; TNBC Triple Negative Breast Cancer

- “Charged” tumors: high levels of CCR4 ligands, T_{reg} and CD8 T cells
- Potential for both monotherapy and combination activity
- Represent cancers with high unmet need and large markets
- Potential for tissue-agnostic accelerated approval in virally-associated tumors

Phase 2: Gated Simon 2-Stage Design

- To evaluate the antitumor activity of FLX475 as monotherapy and in combination with pembrolizumab in charged cancers that progressed after ≥ 1 line of therapy



CPI = Checkpoint Inhibitor

Phase 2: Status and Stage 2 Decisions

Stage 1
N=10
per cohort

Stage 1 Pending

Cervical (CPI Naïve)
Monotherapy

Stage 2
N=19
per cohort

Stage 2 Initiated

EBV⁺ Lymphoma
Mono and Combo

Nasopharyngeal (EBV+)
Combination

Head & Neck (CPI Naïve)
Combination

Head & Neck (CPI Exp.)
Combination

FLX475 Phase 2 Program Summary

- FLX475, a highly selective tumor T_{reg} inhibitor, appears to be an active agent in charged cancers
 - Demonstrated clinical activity as monotherapy
 - Demonstrated clinical activity in combination with pembrolizumab in checkpoint-naïve cancers beyond expected from checkpoint alone
- Ungated Stage 2 expansions in 4 indications
 - EBV+ lymphoma, nasopharyngeal and head and neck cancers (CPI naïve and CPI refractory)
- Favorable safety supportive of broad combinability
- Targeting a medical conference in 2022 for data presentation

Key Takeaways and Upcoming Milestones

- **RPT193**: safe oral agent designed for a broad range of inflammatory diseases with positive Phase 1b data in AD
- **FLX475**: a highly selective tumor T_{reg} inhibitor in multiple Phase 2 expansions as monotherapy and in combination with pembrolizumab
- **Planned Key Milestones**
 - **1H 2022**: RPT193 Phase 2b AD trial initiation
 - **2H 2022**: RPT193 Phase 2a asthma trial initiation
 - **2022**: FLX475 Phase 2 data update



Thank You

