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Oral Drugs Targeting Critical Immune Drivers of Disease



RPT193 (Inflammation):

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

FLX475 (Oncology): • MERCK (Hanni)

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

HPK1 (Oncology)

Other Targets



Proprietary Drug Discovery and Development Engine

Rapid **Analytics**

- Drug discovery
- Clinical development to POC



Interrogating clinically-relevant big datasets to identify targets and biomarkers



Patient selection

Driven by data to improve chances of clinical success

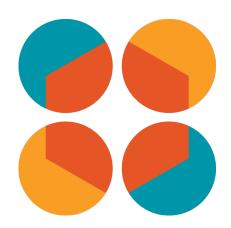


Targeting

Critical immune drivers of cancer and inflammation





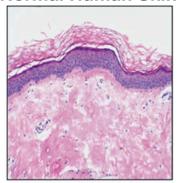


RPT193: CCR4 Antagonist for Inflammatory Diseases

RPT193: Oral CCR4 Antagonist for Inflammatory Diseases

- RPT193 is a highly potent and selective once-daily oral CCR4 antagonist that targets inflammation more specifically than JAK inhibitors and acts upstream of many injectables
- 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



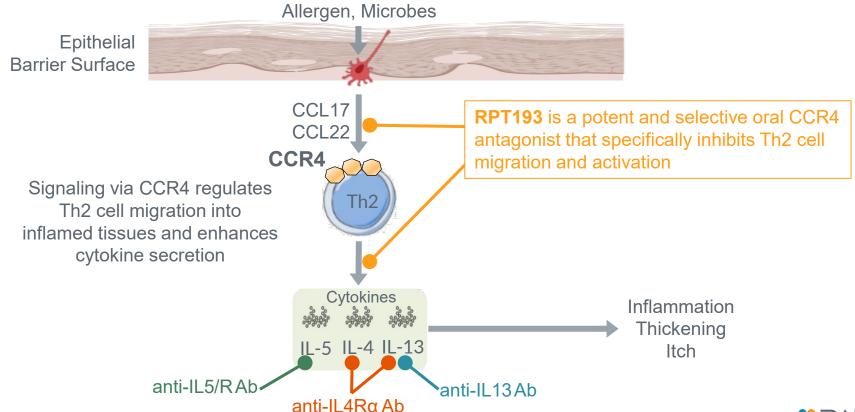
AD Lesional Skin







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*

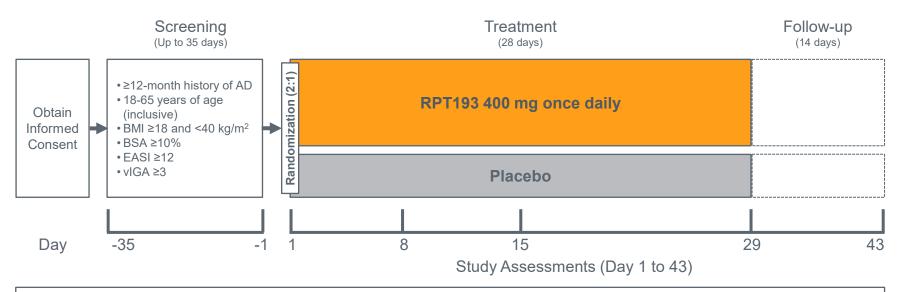
Asthma

- 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 Monotherapy 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



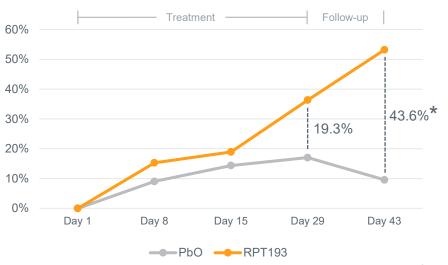
Phase 1b Baseline Demographics and Disease Characteristics

	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 ≥4, n (%)	9 (90.0%)	20 (95.2%)

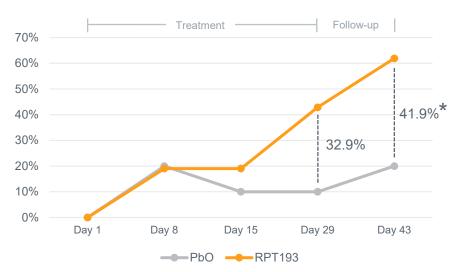


RPT193 Differentiated from Placebo for EASI and EASI-50 at Day 29 with Further Improvement at Day 43

% Improvement in EASI



Proportion of EASI-50

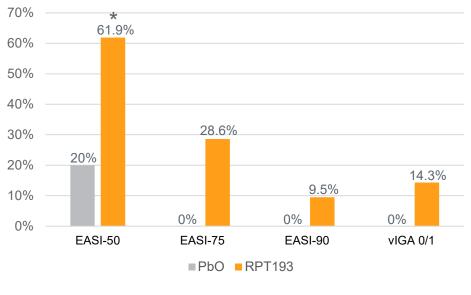






RPT193 Differentiated from Placebo on EASI-75, 90 and vIGA 0/1 at Day 43

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

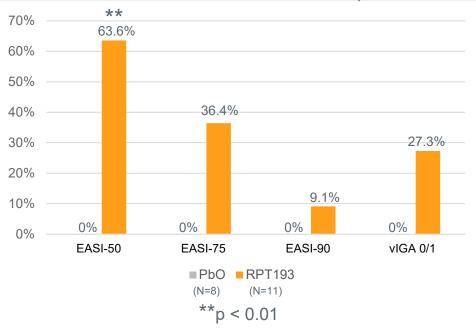


p < 0.05



RPT193 Differentiated from Placebo in Patients with Baseline EASI≥16 at Day 43

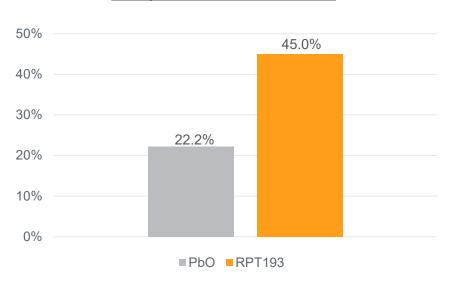
Proportion of EASI-50, 75, 90 and vIGA 0/1 (Clear/Almost Clear)





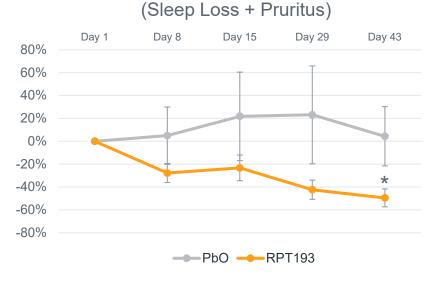
RPT193 Demonstrated Improvement in Itch and Sleep

Proportion of NRS-4[†]



†At least a 4-point improvement among patients with a baseline pruritis NRS ≥4

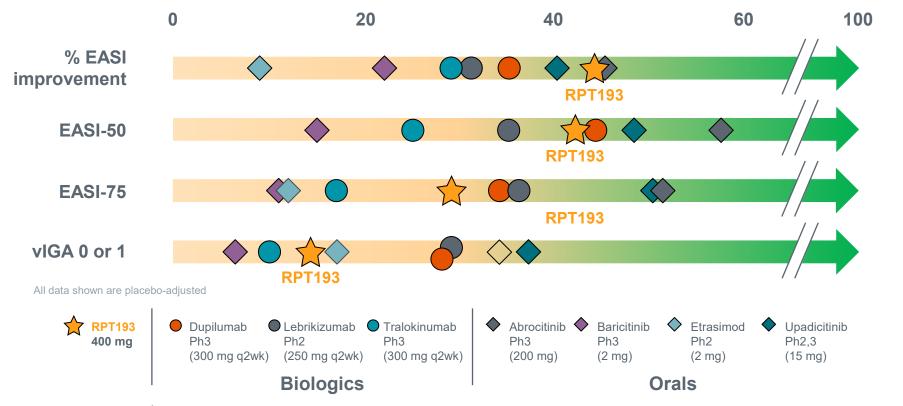
% Change in Subjective SCORAD



p < 0.05



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



^{*} 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

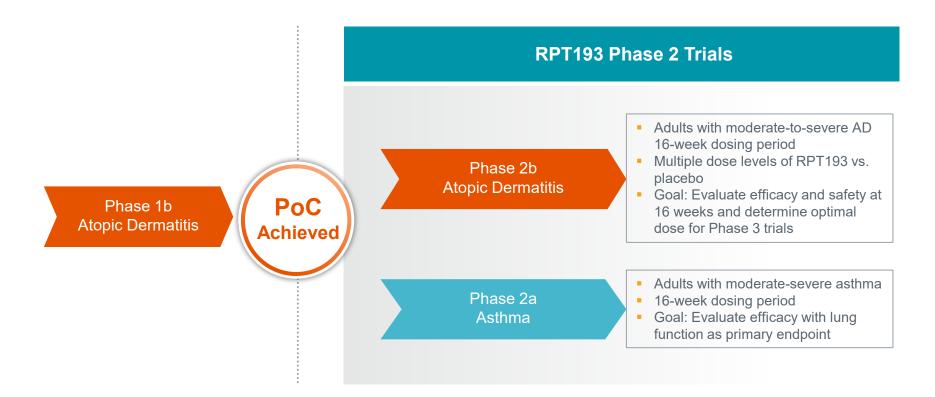


Phase 1b Safety

- 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

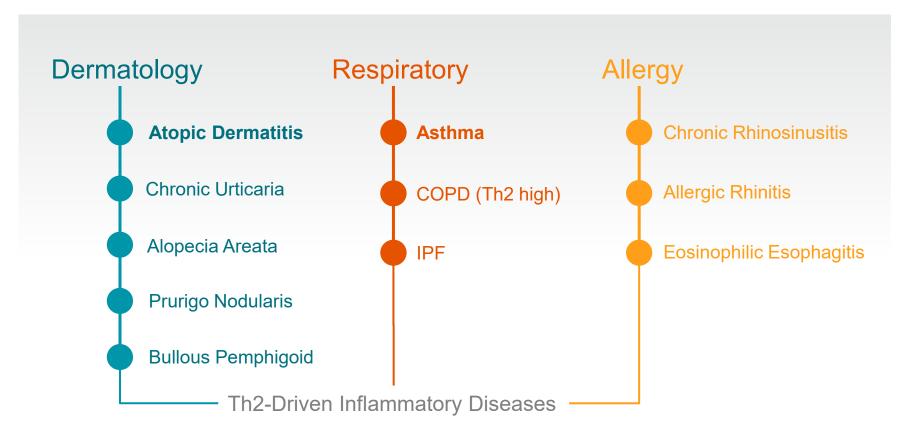


Next Steps for the RPT193 Program





Potential "Pipeline in a Product"

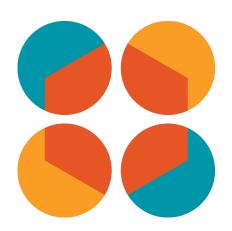




RPT193 Program Summary

- 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 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-tosevere AD and a Phase 2a study in patients with asthma

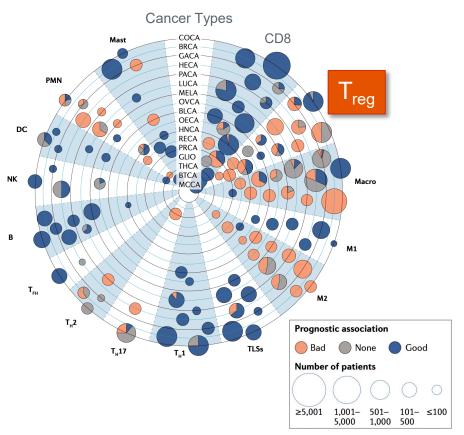




FLX475: CCR4 Antagonist for Oncology

T_{req} are Key Targets in the Tumor Microenvironment (TME)

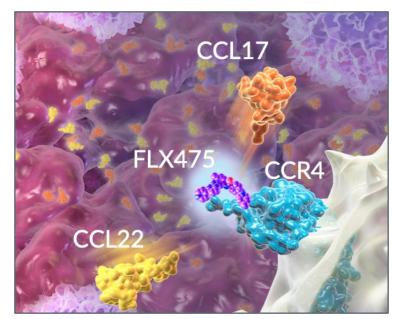
- Correlate with poor prognosis across most cancers
- Mechanism for immune evasion by viruses and tumors
- Barrier to checkpoint inhibitor efficacy
- Challenge: selective inhibition of T_{req} in the TME
 - Depleting antibodies targeting CD25, CCR4, etc., do not appear to have adequate selectivity





FLX475: Oral CCR4 Antagonist in Phase 2

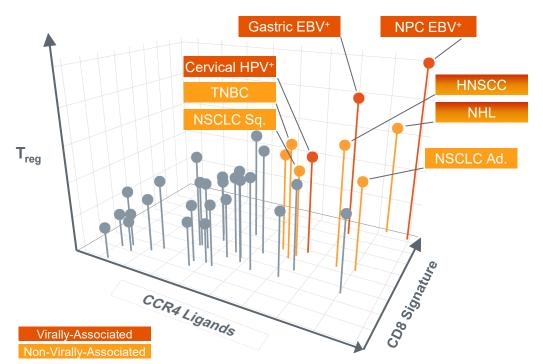
- Highly potent and selective CCR4 small molecule antagonist
- Selectively blocks tumor T_{reg} while sparing normal tissues and beneficial cells
- Potential for superior safety and efficacy compared to depleting antibodies
- Issued U.S. composition of matter patent with coverage through 2037
- Monotherapy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



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



Identification and Characterization of Charged Tumors



- "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 virallyassociated tumors

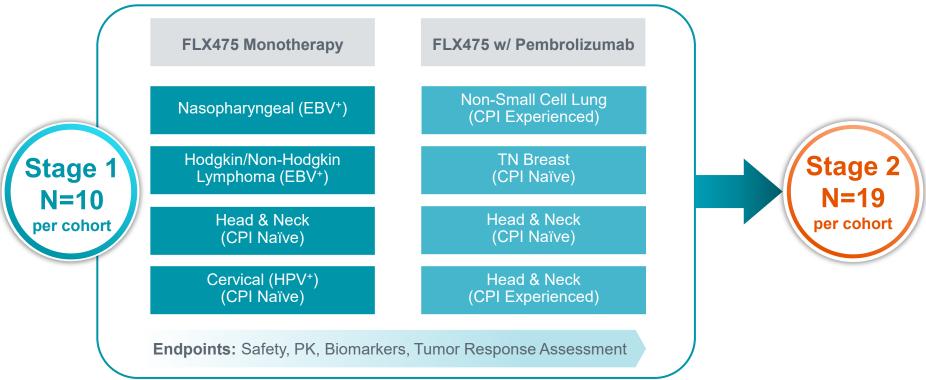
Data from in-house analysis of TCGA database combined with other data sets; Confirmed in > 400 tumor microarrays The graph above reflects a logarithmic scale on each axis

NPC Nasopharyngeal; HNSCC Head & Neck Squamous Cell Carcinoma; NHL Non-Hodgkin Lymphoma; NSCLC Non-Small Cell Lung Cancer; TNBC Triple Negative Breast Cancer

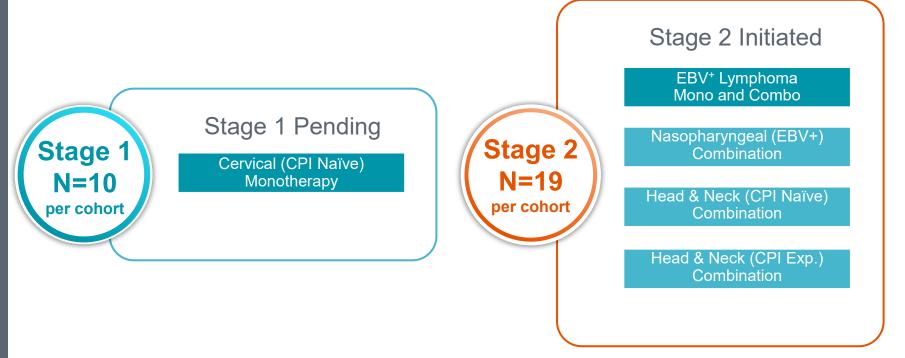


Phase 2: Gated Simon 2-Stage Design

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



Phase 2: Status and Stage 2 Decisions





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 an array of inflammatory diseases – 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 1b AD biomarker data
 - 1H 2022: RPT193 Phase 2b AD trial initiation
 - 2H 2022: RPT193 Phase 2a asthma trial initiation
 - 2022: FLX475 Phase 2 data update



