



# Transforming the Treatment of Cancer and Inflammation

March 2021  
Corporate Presentation

# Legal Disclaimers

Statements in this Presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding RAPT Therapeutics, Inc.'s (the "Company," "we," or "us") research and clinical development plans; current and future drug candidates; business strategy and plans; regulatory pathways; and our ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "will," "may," "upcoming," "milestone," "potential," "target" or the negative of these terms or similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the current beliefs of the Company's management with respect to future events and trends and are subject to known and unknown risks and uncertainties, including those described in the "Risk Factors" section of our most recent Form 10-K or 10-Q filed with the Securities and Exchange Commission, that may cause our actual performance or achievements to be materially different from any future performance or achievements expressed or implied by the forward-looking statements in this Presentation. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that any assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of such assumptions, fully stated in the Presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this Presentation is given. Although we believe that the beliefs and assumptions reflected in the forward-looking statements are reasonable, we cannot guarantee future performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Presentation.

This Presentation discusses drug candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of any drug candidates for any use for which such drug candidates are being studied.

# Oral Drugs Targeting Critical Immune Drivers of Disease

- Proprietary discovery engine
- Diversified pipeline
- Large market opportunities
- Multiple near-term clinical readouts
- Strategic collaborations

CLINICAL

**FLX475** (Oncology):  **MERCK** 

- Selectively targets immunosuppressive tumor  $T_{reg}$
- PoC in Phase 2 with multiple expansions underway
- Monotherapy and combo clinical activity observed
- **Next Phase 2 update 2H 2021**

**RPT193** (Inflammation):

- Oral agent targets inflammatory Th2 cells
- Robust PK/PD with excellent safety in Ph1 study
- **Phase 1b PoC in atopic dermatitis ongoing – data readout in 1H 2021**

DISCOVERY

**HPK1** (Oncology)

**GCN2** (Oncology)

# Proprietary Drug Discovery and Development Engine

R

Rapid

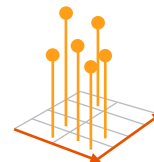
- Drug discovery
- Clinical development to POC



A

Analytics

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



P

Patient selection

- Driven by data to improve chances of clinical success



T

Targeting

- Critical immune drivers of cancer and inflammation

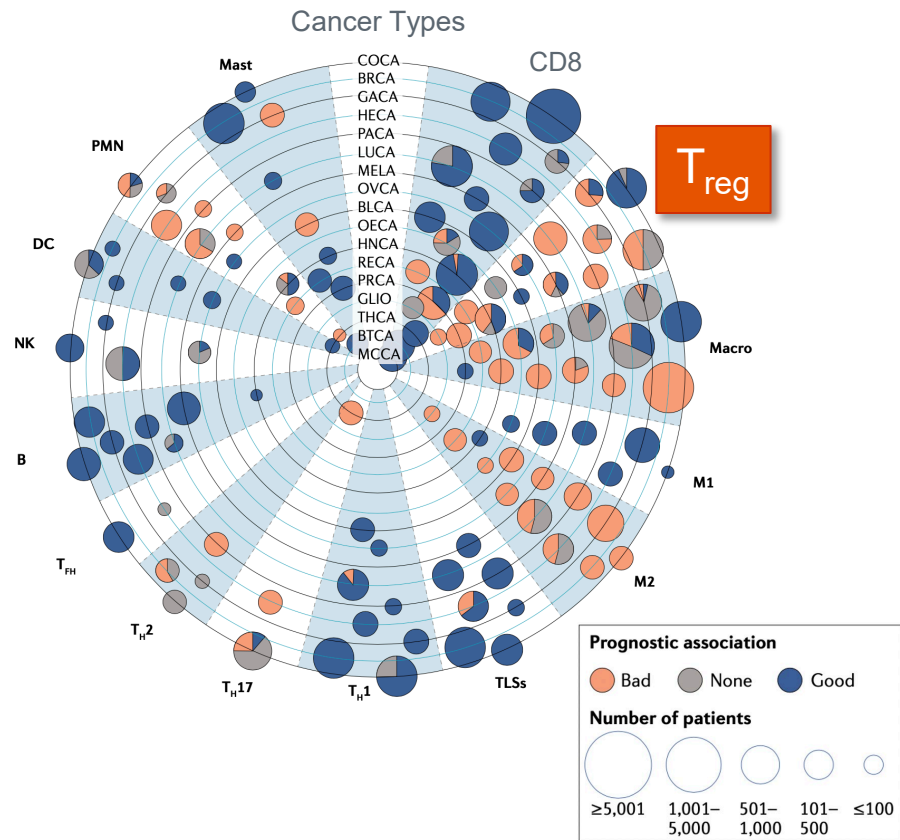




# FLX475: CCR4 Antagonist for Oncology

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

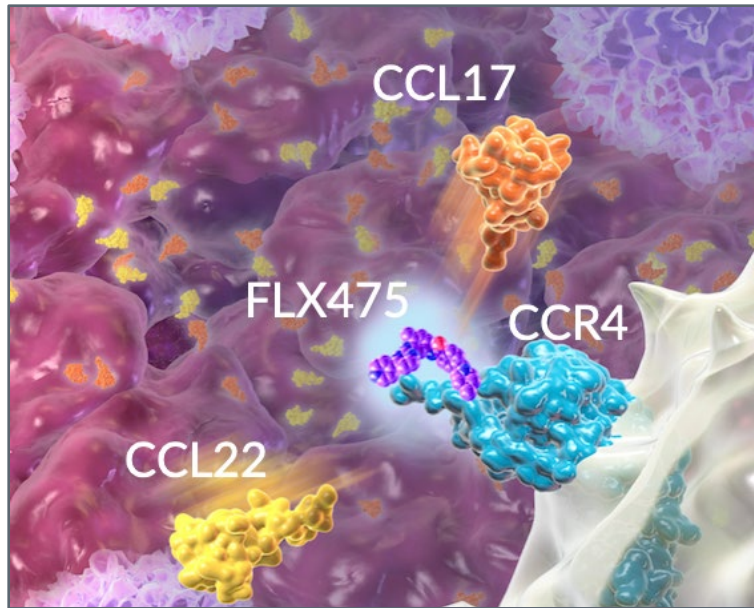
- Correlate with poor prognosis across most cancers
- Mechanism for immune evasion by viruses and tumors
- Barrier to checkpoint inhibitor efficacy
- Challenge: selective inhibition of  $T_{reg}$  in the TME
  - Depleting antibodies targeting CD25, CCR4, etc. do not appear to have adequate selectivity





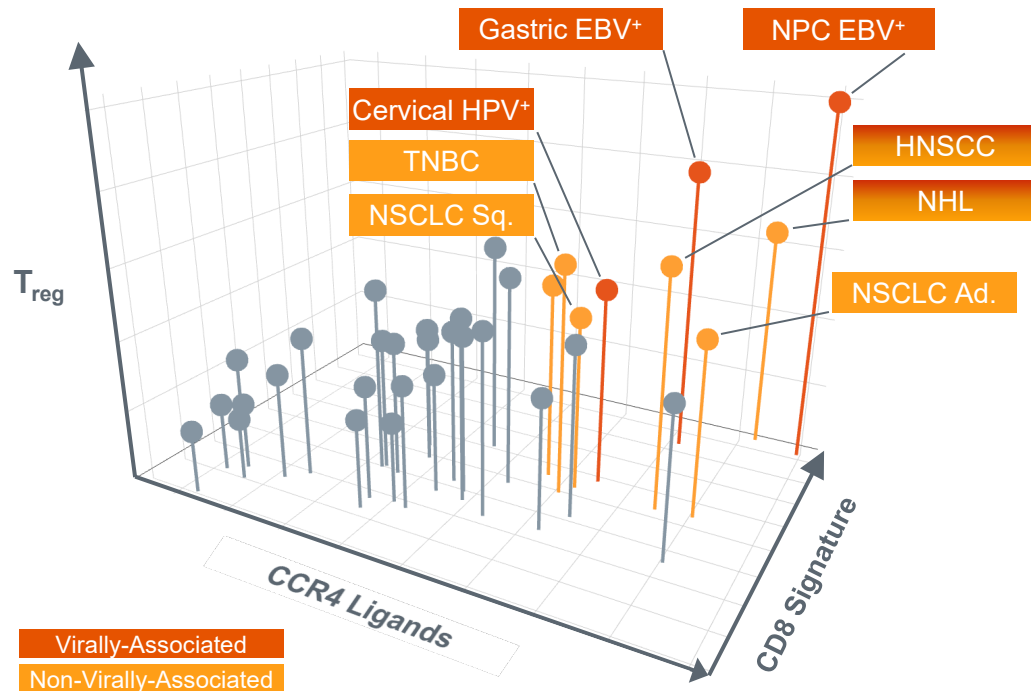
# FLX475: Oral CCR4 Antagonist in Phase 2

- 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



# A Large Proportion of Multiple Tumor Types Are Charged

Tumor Type	Prevalence* (U.S.)	Virally Associated	Percent Viral	Estimated Percent Charged**
Non-Small Cell Lung Cancer	268,600	N/A	N/A	60-80%
Triple Negative Breast Cancer	145,500	N/A	N/A	
Head and Neck Squamous Cell Carcinoma	143,000	✓	25%-60%	
Nasopharyngeal Cancer	105,000***	✓	>95%	>90% of virally associated tumors
Cervical Cancer	46,800	✓	>95%	
EBV+ Lymphoma	28,700****	✓	100%	> 90%

\* Based on 2012 Globocan registries 5-year prevalence (2008-2012 estimates)

\*\* Data from in-house analysis

\*\*\* World-wide prevalence

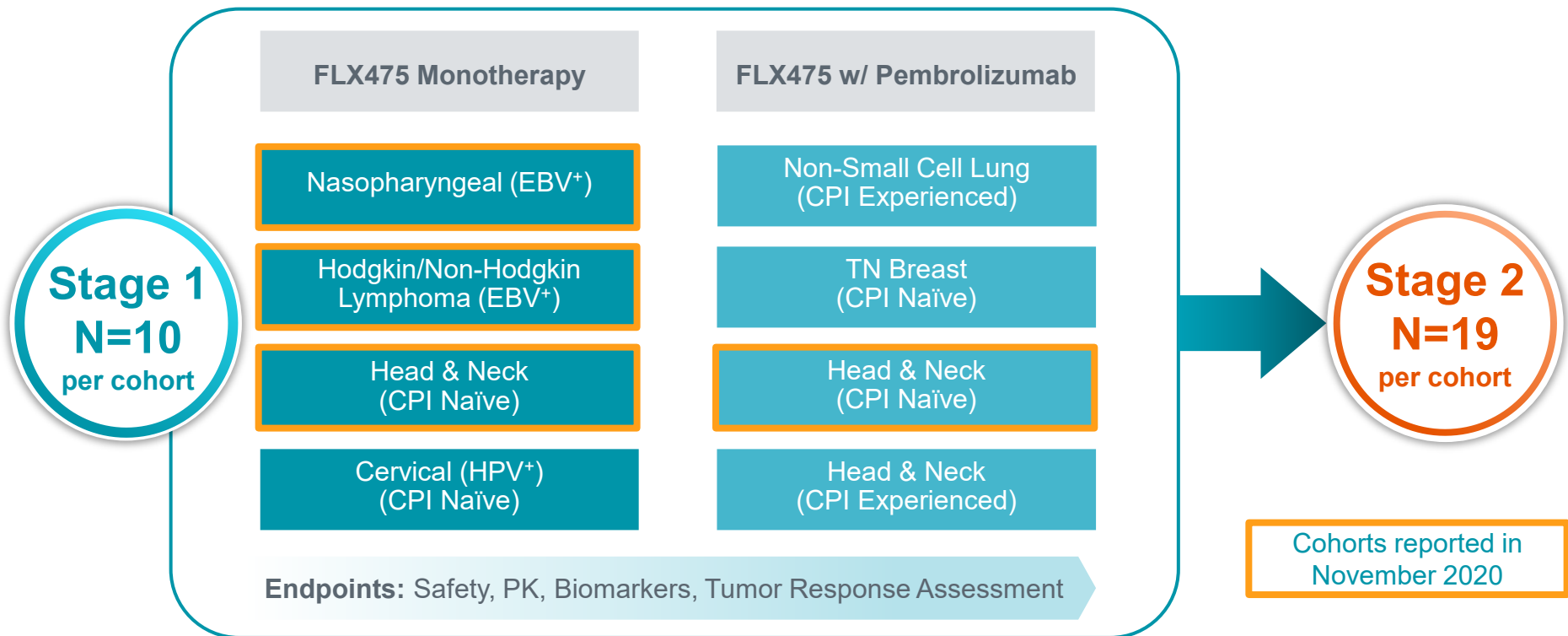
\*\*\*\* Estimated based on 2018 Globocan registries 5-year prevalence (2013-2018 estimates and Heslop, H., American Society of Hematology 2005, 260-266)

# Phase 1 Dose Escalation Summary

- Standard 3+3 dose escalation of monotherapy and in combination in non-charged and charged cancers
- 37 patients enrolled, 4 remain on study (12-18 months)
- Favorable safety with no overlapping toxicities with pembrolizumab
- Tumor biomarker changes supportive of  $T_{reg}$  mechanism
- 100 mg QD selected as the Phase 2 dose
- Preliminary evidence of monotherapy and combination clinical activity in heavily pretreated charged tumor types
  - 1 unconfirmed partial response in monotherapy (cervical)
  - 2 partial responses in combination (1 in PD-L1 refractory NSCLC, 1 in CPI-naïve bladder)

## 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  $\geq 1$  line of therapy



CPI = Checkpoint Inhibitor

# Predefined Success Criteria for Phase 2 Stage 1

## Monotherapy

- Any monotherapy activity would be considered highly encouraging in this small trial
  - Most IO agents have failed to clearly demonstrate monotherapy activity
  - Demonstrates activity: important to interpret combination data
- Robust monotherapy activity could permit a single agent path in some indications and settings

## Combination

- Activity above expected from checkpoint inhibition alone
  - Checkpoint naïve - varies
  - Checkpoint experienced – less than 5-10%

Overlay clinical judgement based on depth and durability of responses

# Phase 2 Trial Update: Key Findings

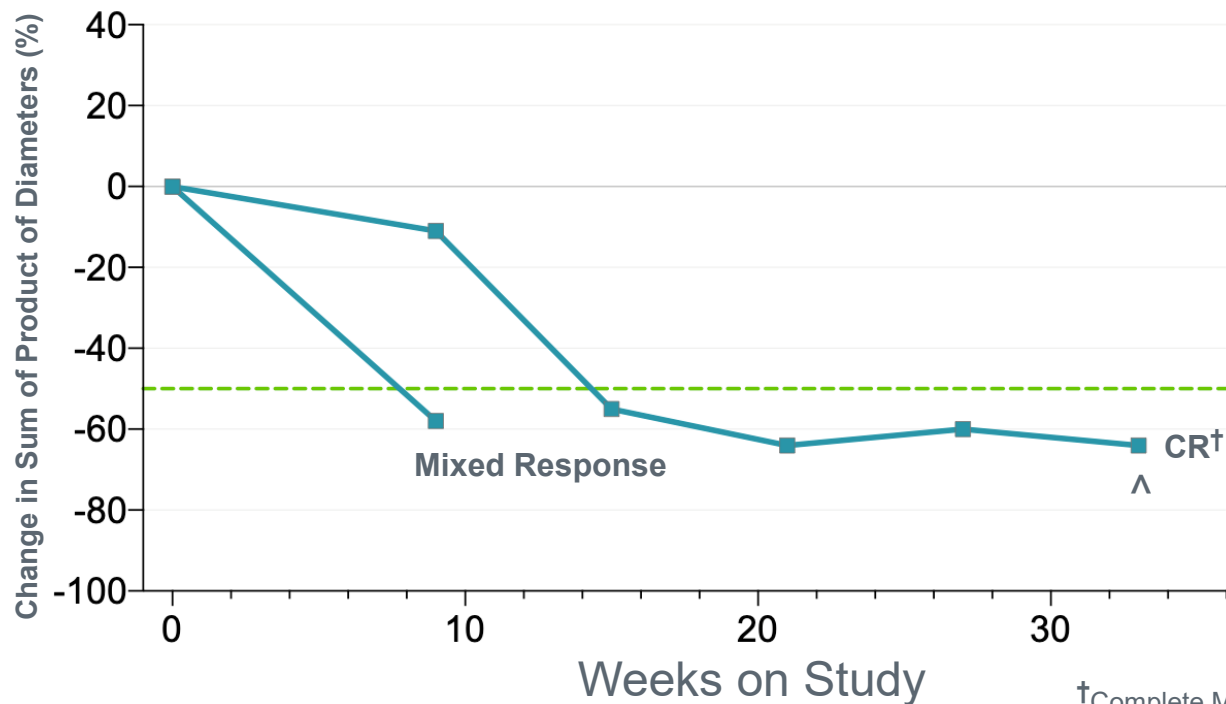
Tumor Type	Observations	Decision
EBV <sup>+</sup> Hodgkin/Non-Hodgkin Lymphoma	Deep and durable response to FLX475 monotherapy	<ul style="list-style-type: none"><li>Expand monotherapy cohort</li><li>Expand a combination cohort</li></ul>
Nasopharyngeal Carcinoma (NPC)	Frequent and deep responses in CPI-naïve patients in combination	<ul style="list-style-type: none"><li>Expand a combination cohort</li></ul>
Head & Neck Squamous Cell Carcinoma (HNSCC)	Multiple responses in CPI-naïve patients in combination including a confirmed CR	<ul style="list-style-type: none"><li>Expand combination cohort</li></ul>

- Favorable safety profile with once-daily oral dosing both as monotherapy and in combination with pembrolizumab

This combined Phase 1/2 study is ongoing. Data are as of 11/10/2020 and findings and conclusions subject to change as more data accumulate and the study is completed.

# EBV<sup>+</sup> Lymphoma: Monotherapy Activity Observed

First 2 of 2 EBV<sup>+</sup> lymphoma patients enrolled experienced significant reduction in size of target lesions, including one with durable complete metabolic response (PET)



- Both are EBV<sup>+</sup> NHL subtypes and are charged
- Compelling monotherapy activity observed supports enrollment of full Stage 2 cohort
- Plan to explore combination activity in parallel

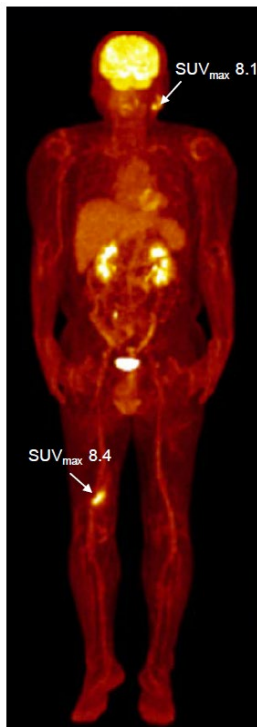
<sup>†</sup>Complete Metabolic Response

<sup>^</sup>Remains on study

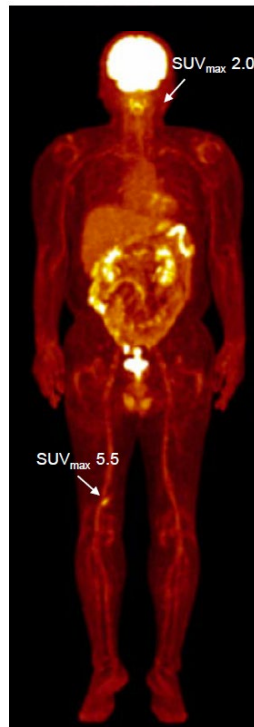
# EBV<sup>+</sup> NHL Case: Complete Metabolic Response to FLX475 Monotherapy

- EBV<sup>+</sup> NK/T NHL
  - 53 y/o, 2L with prior chemotherapy 1H 2019
  - 2 primary lesions
    - L posterior auricular (target), R distal anterior thigh (non target)
- Deep Durable Response
  - 8-week scan with complete metabolic response (Deauville score of 5 reduced to 2) and target lesion visibly improving by 12 weeks
  - Patient remains in complete metabolic response and on study > 9 months

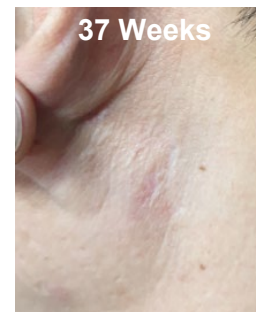
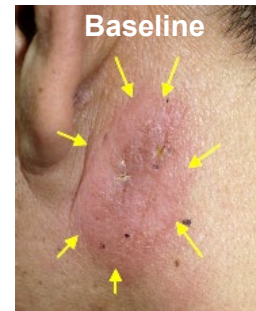
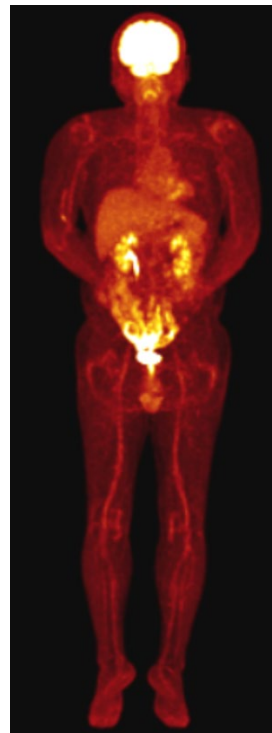
Baseline PET



8 Weeks

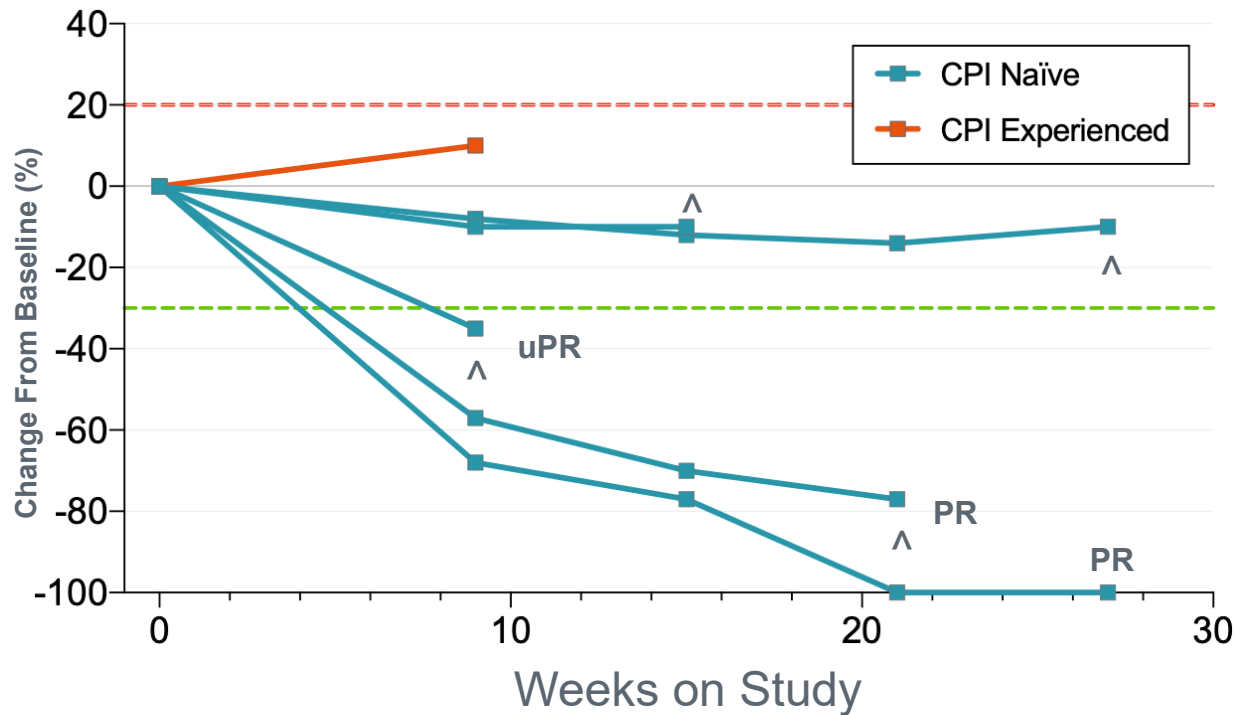


33 Weeks





# NPC Crossover: 5/5 CPI-naïve Patients with Tumor Shrinkage, 3/5 with Unconfirmed or Deep PR

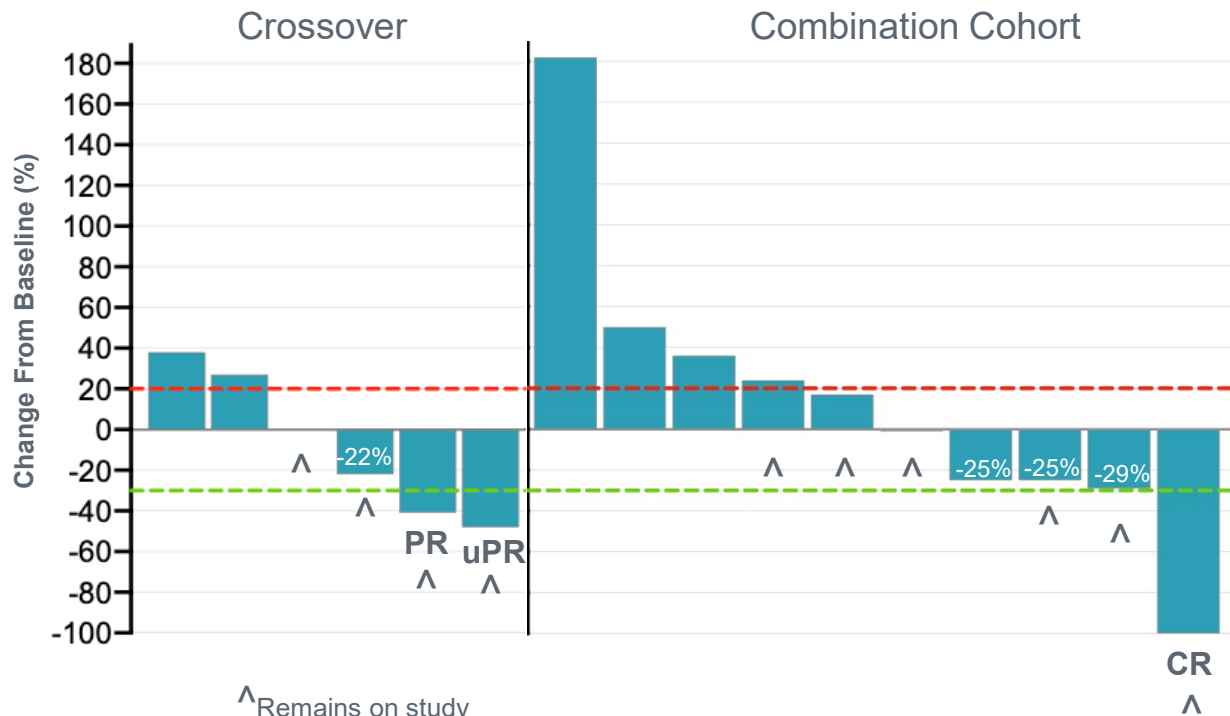


- 6 evaluable crossover patients, 5 CPI-naïve
  - 5/5 tumor shrinkage, including 1 uPR and 2 deep PRs
- ORR of pembrolizumab alone in CPI-naïve NPC is 26% (all PRs)<sup>1</sup>
- Data support further exploration of combination in patients with CPI-naïve NPC

^ Remains on study

<sup>1</sup>Hsu et al. (2017) J Clin Oncol 35:4050-4056 (KEYNOTE-028)

# HNSCC CPI-Naïve: Promising Combination Activity (Best Response on Study)



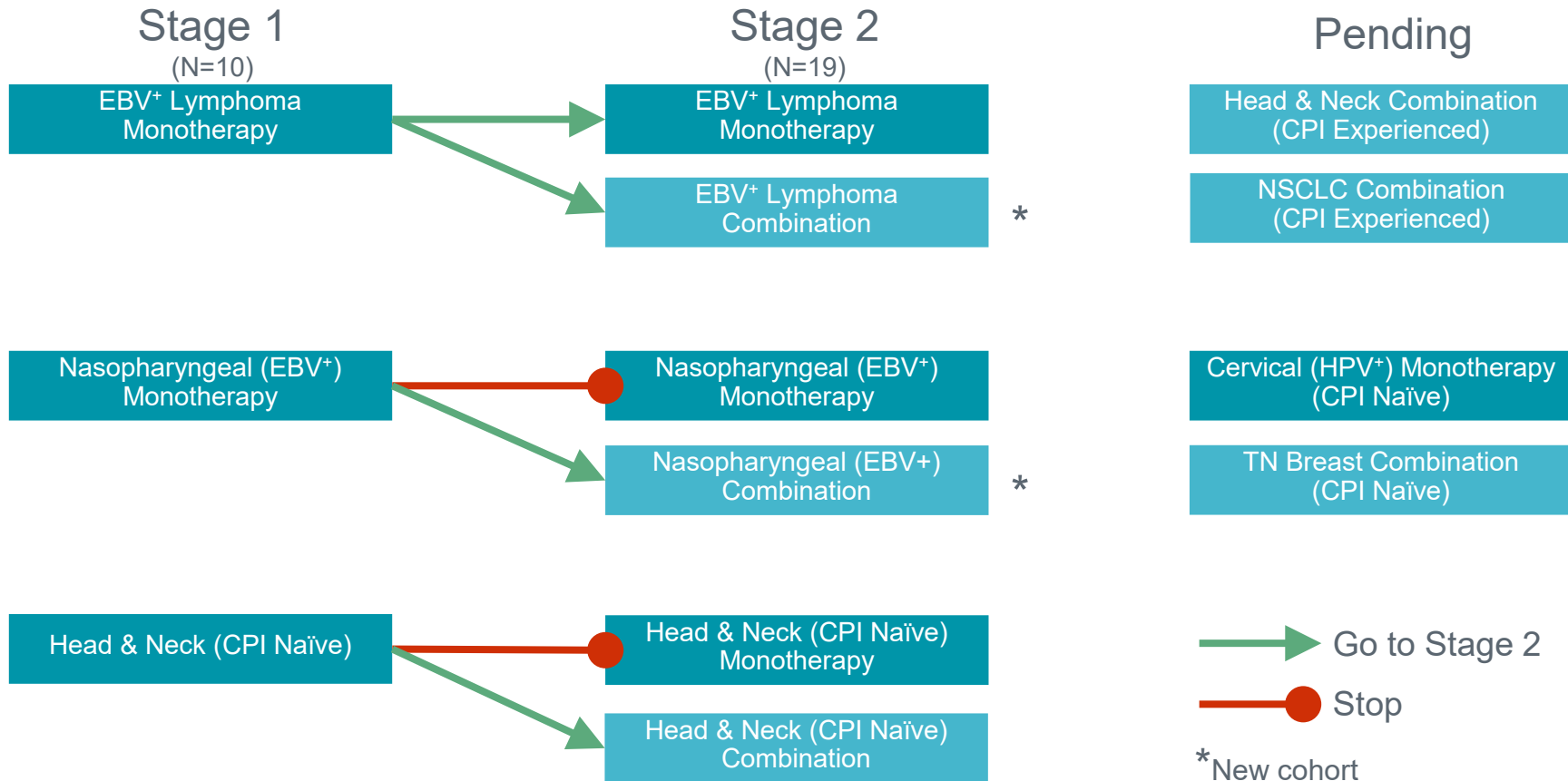
<sup>1</sup>Bauml et al. (2017) J Clin Oncol 35: 1542-49 (KEYNOTE-055)

- Crossover
  - 6 enrolled and evaluable
  - 1 PR, 1uPR, 2 SD (1 with target reduction > 20%), 2 PD
- Combination Cohort
  - 17 enrolled; 10 evaluable
  - 1 CR, 5 SD (3 with target reduction > 20%), 4 PD
- ORR of pembrolizumab alone in CPI-naïve HNSCC is 16% (CR rate <1%)<sup>1</sup>
- Level of activity and totality of data support full Stage 2 CPI-naïve combination cohort

## Phase 2 Safety

- No new significant safety findings vs Phase 1
  - No evidence of increased severity or frequency of AEs in combination therapy vs either FLX475 or pembrolizumab given alone
  - Asymptomatic and reversible QTc prolongation continues to be the primary FLX475-related finding
- Serious adverse events potentially related to study treatment in the Phase 2 patients initially reported on (44 patients, 4 cohorts)
  - 1 QTc prolongation (asymptomatic) in a patient on monotherapy
  - 1 episode of colitis and concurrent renal insufficiency in one patient on combination therapy

# Phase 2: Stage 2 Decisions



# FLX475 Program Summary

- FLX475, a highly selective tumor  $T_{reg}$  inhibitor, appears to be an active agent in charged cancers
  - Demonstrated clinical activity of FLX475 as monotherapy
  - Demonstrated clinical activity of FLX475 in combination with pembrolizumab in checkpoint-naïve cancers beyond expected from checkpoint alone
  - Expanded multiple cohorts in EBV+ lymphoma, nasopharyngeal and head and neck cancers
- Favorable safety supportive of broad combinability
- Next data update planned in 2H 2021

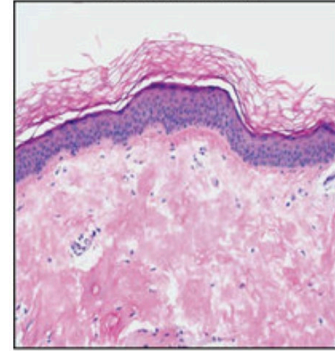


# RPT193: CCR4 Antagonist for Inflammatory Diseases

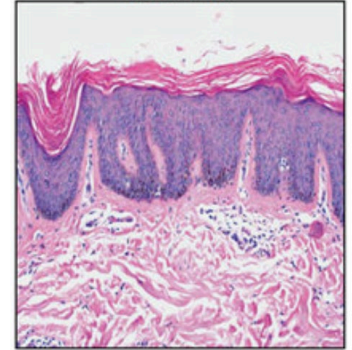
# RPT193: Oral CCR4 Antagonist for Inflammation

- Targeting atopic dermatitis, asthma, others
- Oral convenience could provide substantial competitive advantage to injectables and topical agents
  - e.g., Apremilast (Otezla) in psoriasis
- Preclinical studies and healthy volunteer data suggest an excellent safety profile
  - No monitoring or black box warning expected
- Phase 1b trial ongoing in atopic dermatitis patients with PoC readout in 1H 2021

Normal Human Skin

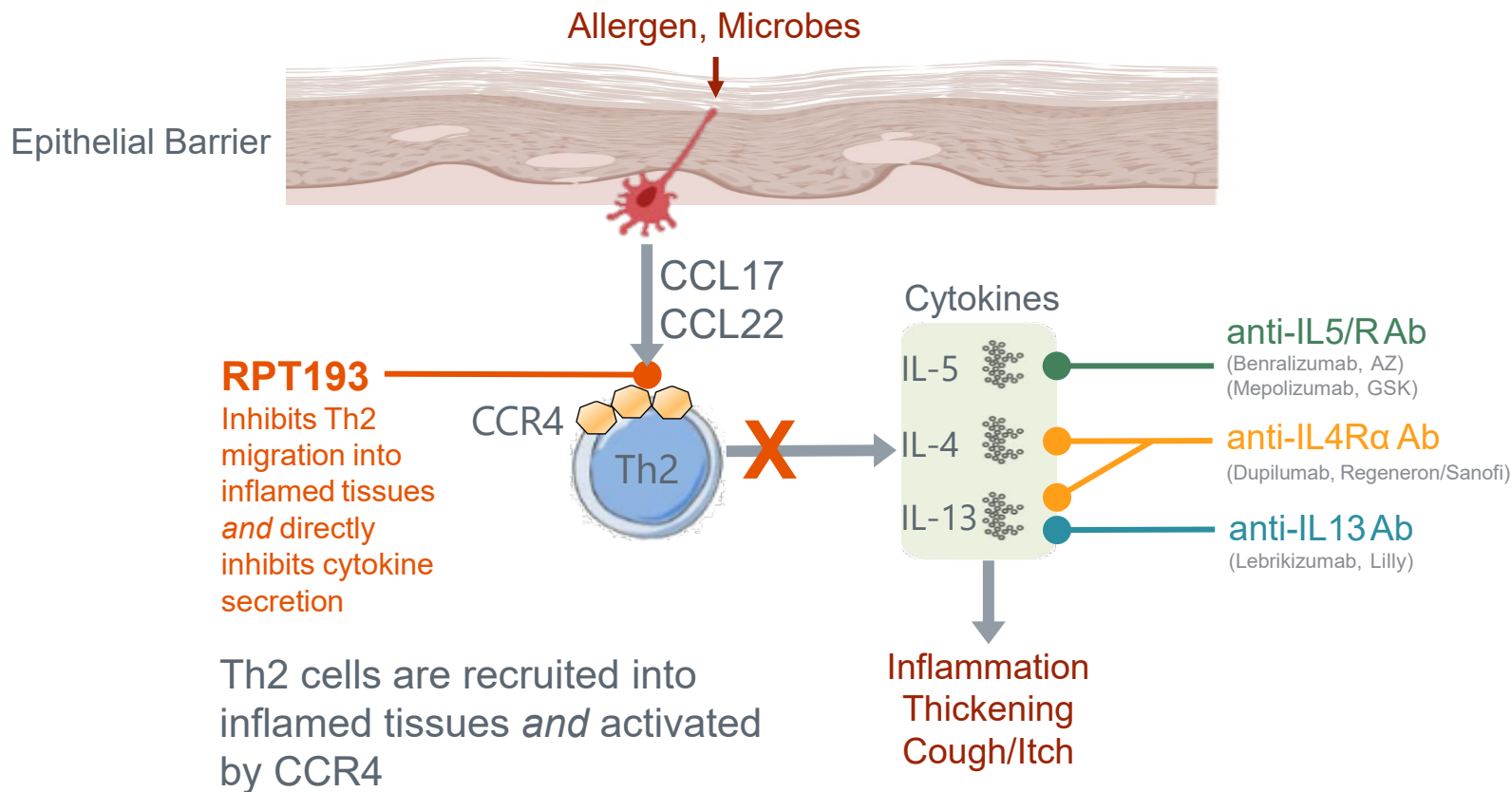


AD Lesional Skin

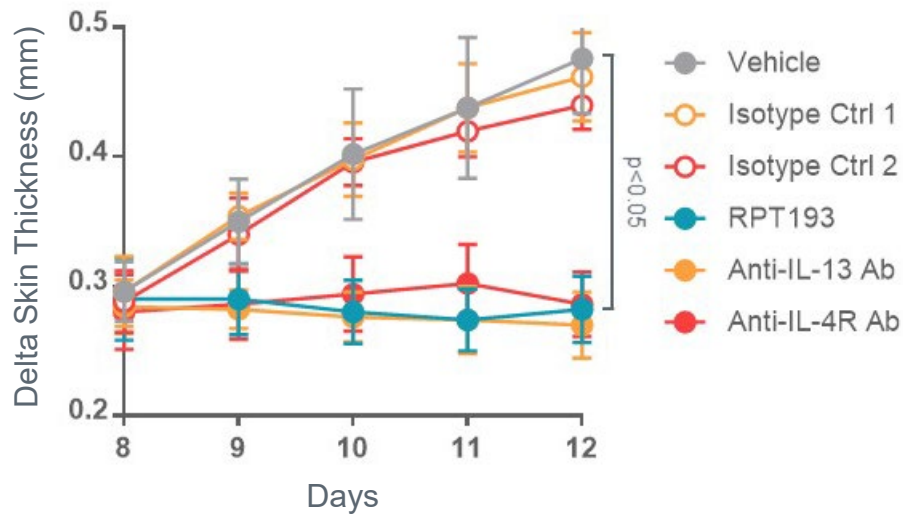
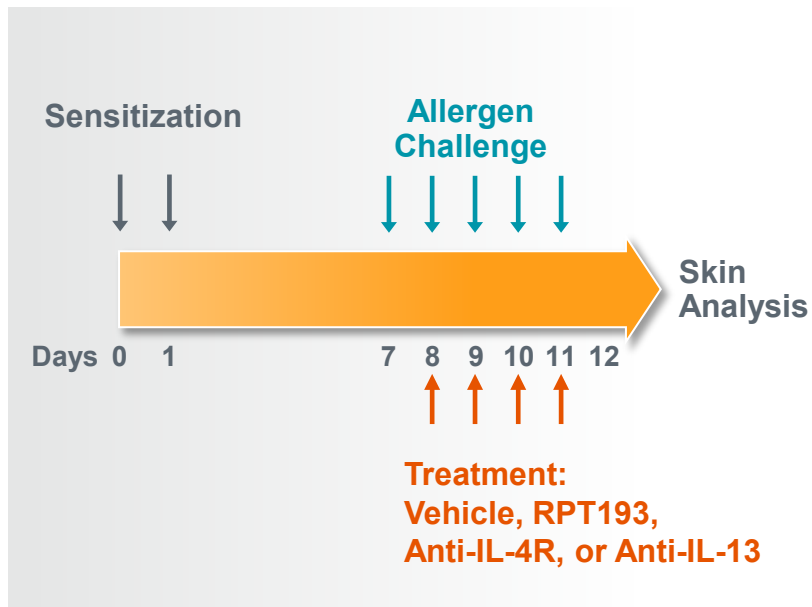




# RPT193 Acts on the Well Known Th2 Pathway in Inflammation

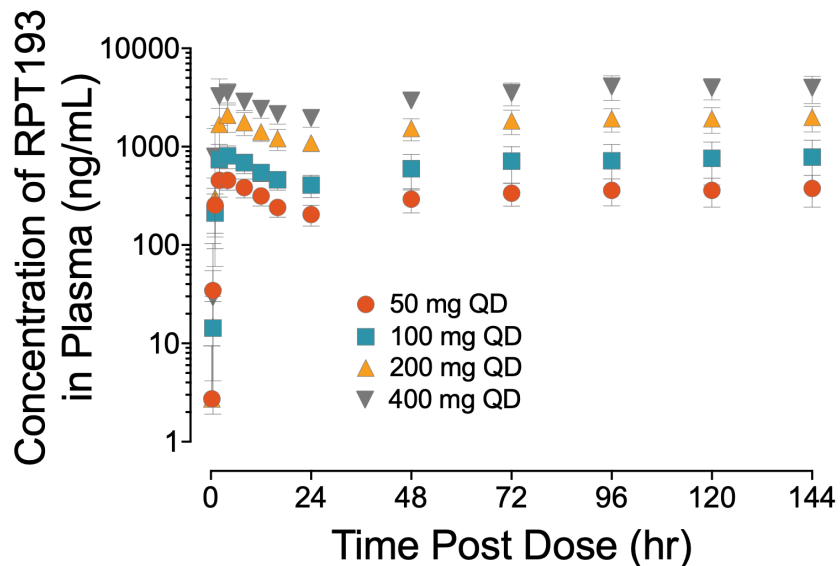


# RPT193 Reduces Skin Inflammation in a Therapeutic Th2-Driven Atopic Dermatitis Model

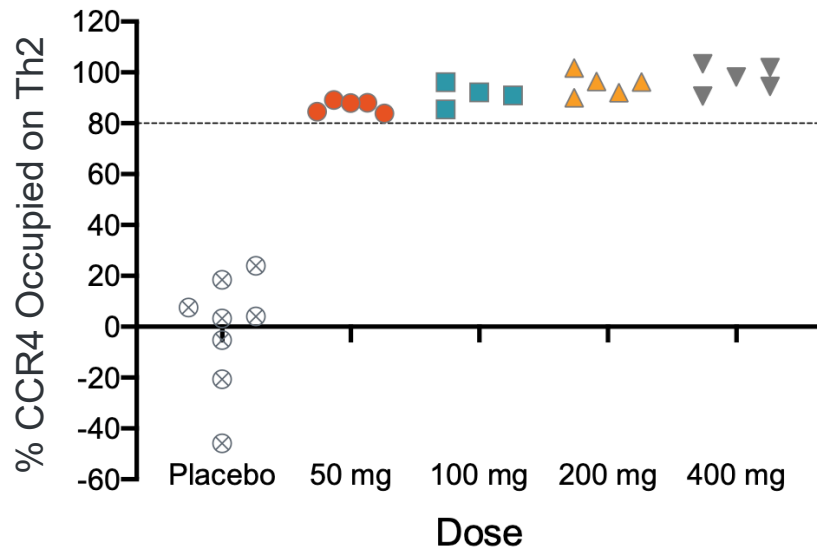


# Phase 1a Healthy Volunteer Data Support Once-Daily Dose

## Dose-Proportional Oral PK with ~24 Hr. Half-Life

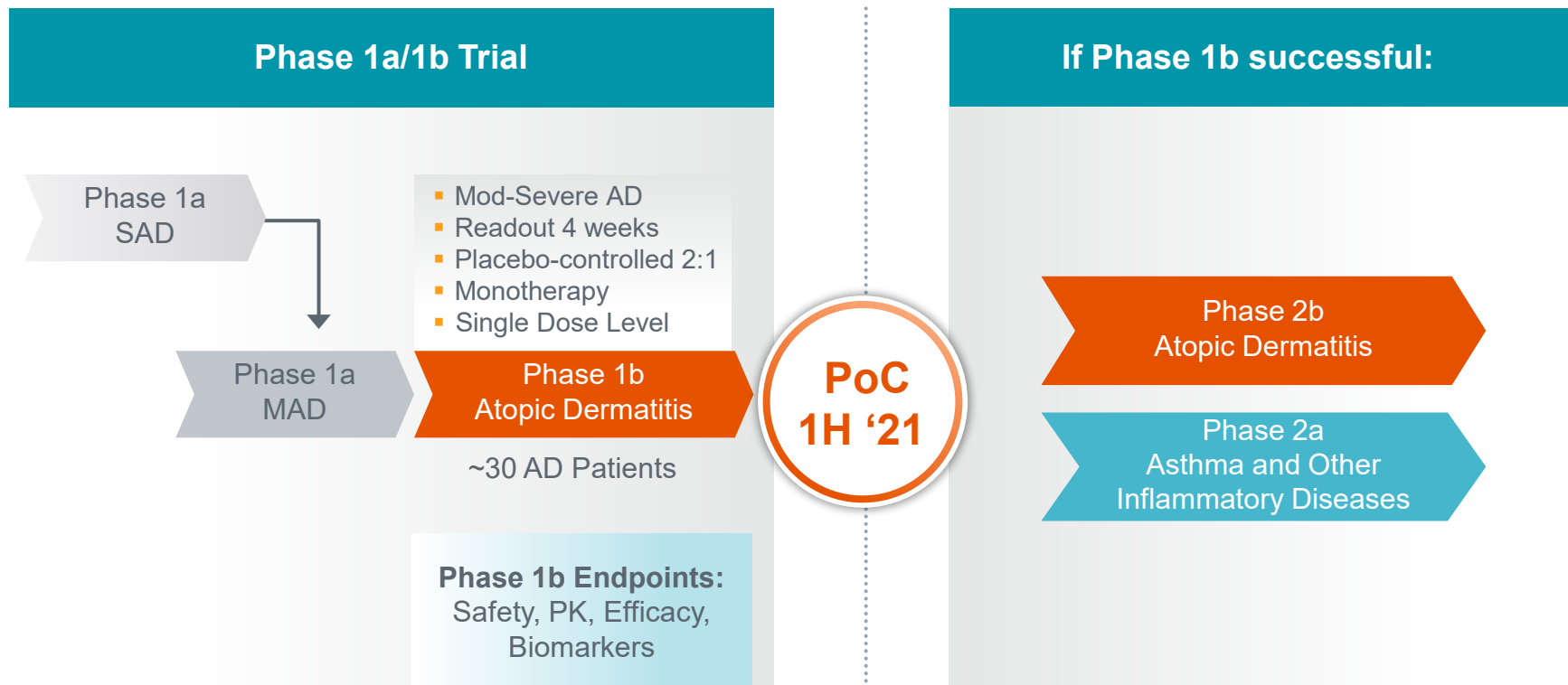


## Targeted Level of CCR4 Inhibition Exceeded Day 8 trough after last dose



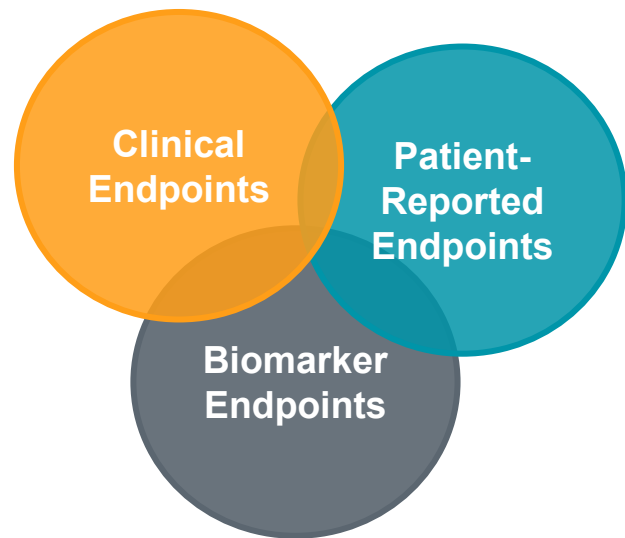
- Excellent safety and tolerability profile (blinded)

# Development Plan in Atopic Dermatitis, Asthma and Other Inflammatory Diseases

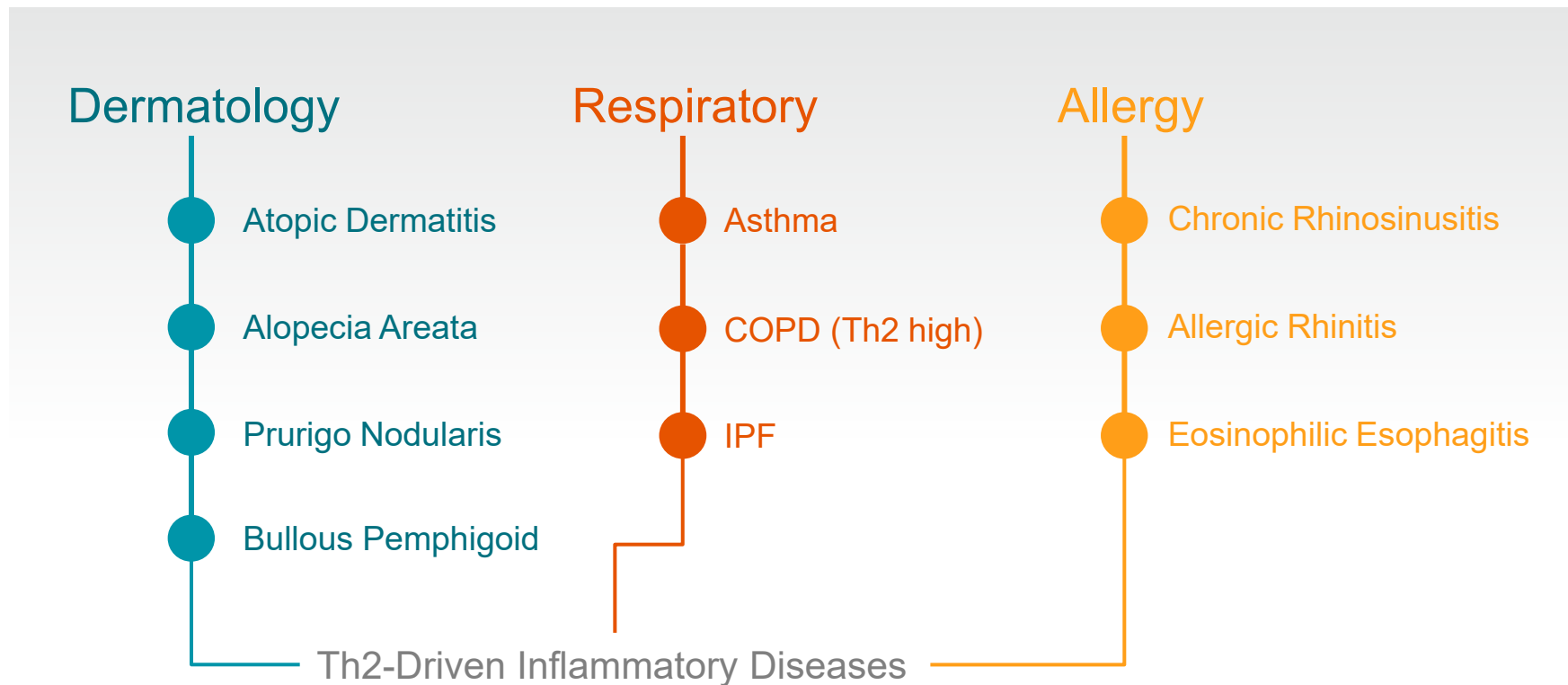


# Goals for the Phase 1b Trial

- Phase 1b is exploring a range of clinical, patient-reported, and biomarker endpoints
  - e.g., EASI, vIGA, Itch NRS, serum CCL17
  - Trial not statistically powered on any specific measure
- An encouraging outcome would be data consistent with an effective oral agent that requires no safety monitoring, analogous to Otezla in psoriasis
  - A clear benefit (change from placebo) from RPT193 in at least one key clinical or patient-reported endpoint
  - Magnitude would not need to be similar to injectables
  - Potential positioning ahead of injectables



# Potential “Pipeline in a Product”



# Key Takeaways and Upcoming Milestones

- **FLX475**: a highly selective  $T_{reg}$  inhibitor with demonstrated clinical activity as monotherapy and in combination – PoC established
- **RPT193**: safe oral agent in a well known pathway for atopic dermatitis, asthma and other allergic disorders
- **Next Key Milestones**
  - **1H 2021**: RPT193 Phase 1b PoC data in atopic dermatitis
  - **2H 2021**: FLX475 Phase 2 update





**Thank You**