



Transforming the Treatment of Inflammation and Cancer

January 2023
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 targeting inflammatory Th2 cells
- Phase 1b in AD: efficacy on all key exploratory endpoints with excellent safety and tolerability
- Phase 2b in AD ongoing, data expected Q4 2023
- Plan to initiate Phase 2a in Asthma Q1 2023

FLX475 (Oncology): MERCK

- Selectively targets immunosuppressive tumor T_{reg}
- PoC in Phase 2 with mono and combo activity
- Phase 2 data update expected 2H 2023

DISCOVERY

HPK1 (Oncology)

Other inflammation and oncology targets

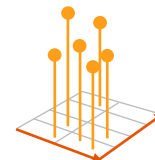
Proprietary Drug Discovery and Development Engine



- Drug discovery
- Clinical development



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



- Driven by data to improve chances of clinical success



- Critical immune drivers of cancer and inflammation



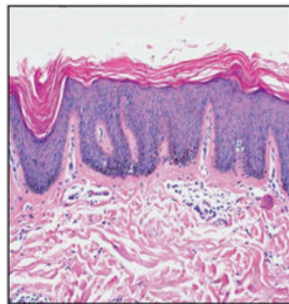


RPT193: CCR4 Antagonist for Inflammatory Diseases

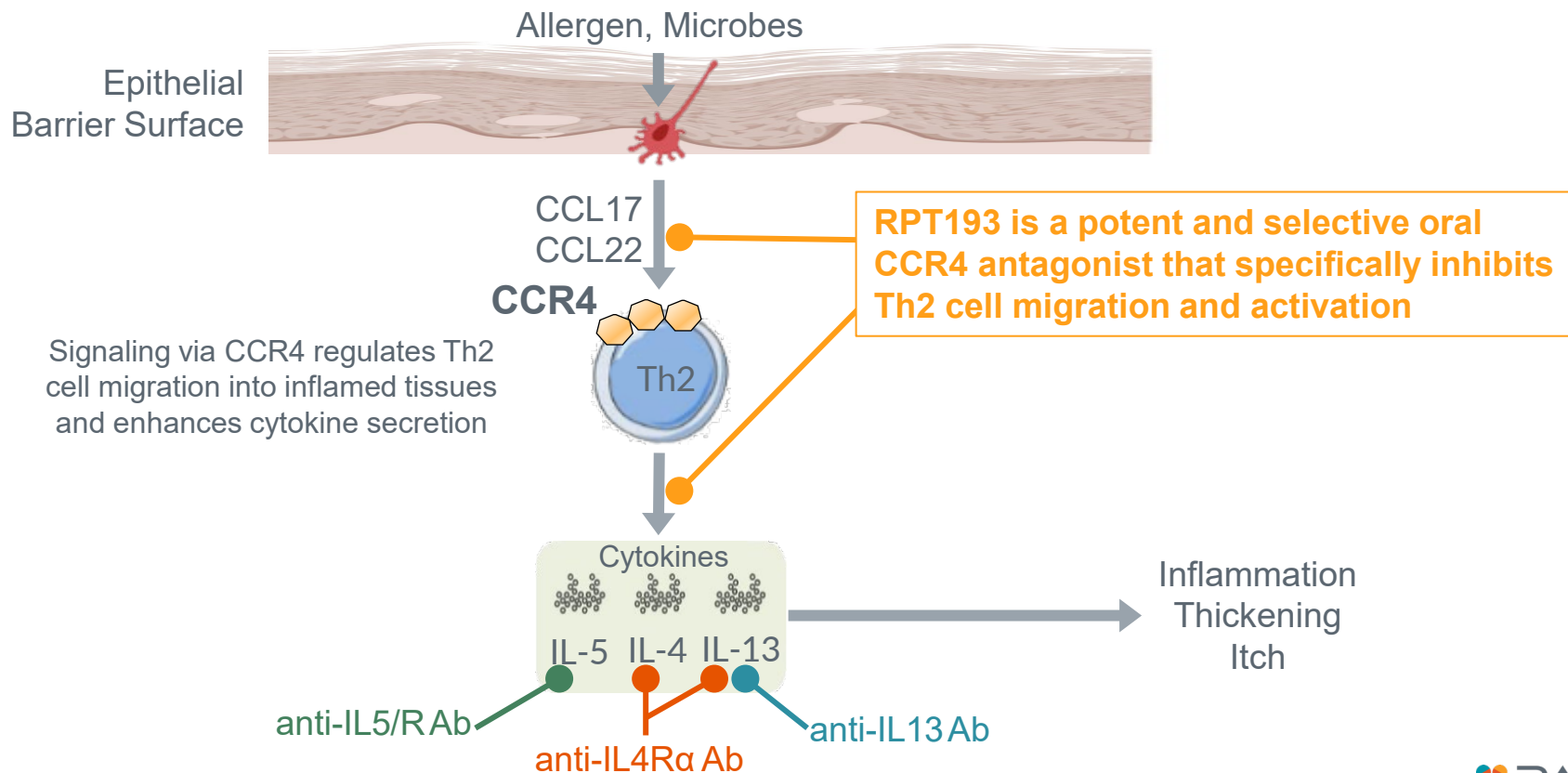
RPT193: Oral Th2 Inhibitor for Inflammatory Diseases

- **Highly potent and selective once-daily oral** CCR4 antagonist designed to safely reduce Th2-inflammation in a broad range of allergic disorders
- **Clear benefit on signs and symptoms** in Phase 1b in moderate-to-severe atopic dermatitis
- **Favorable safety and tolerability:** no laboratory safety monitoring or black box warning expected
- **Potential positioning as drug of first choice** after inadequate response to TCS and prior to injectables
- **US patent coverage through at least 2039**
- **Phase 2b AD data expected Q4 2023** and pivotal studies anticipated to start in 2024
- **Plan to initiate Phase 2a asthma trial Q1 2023**

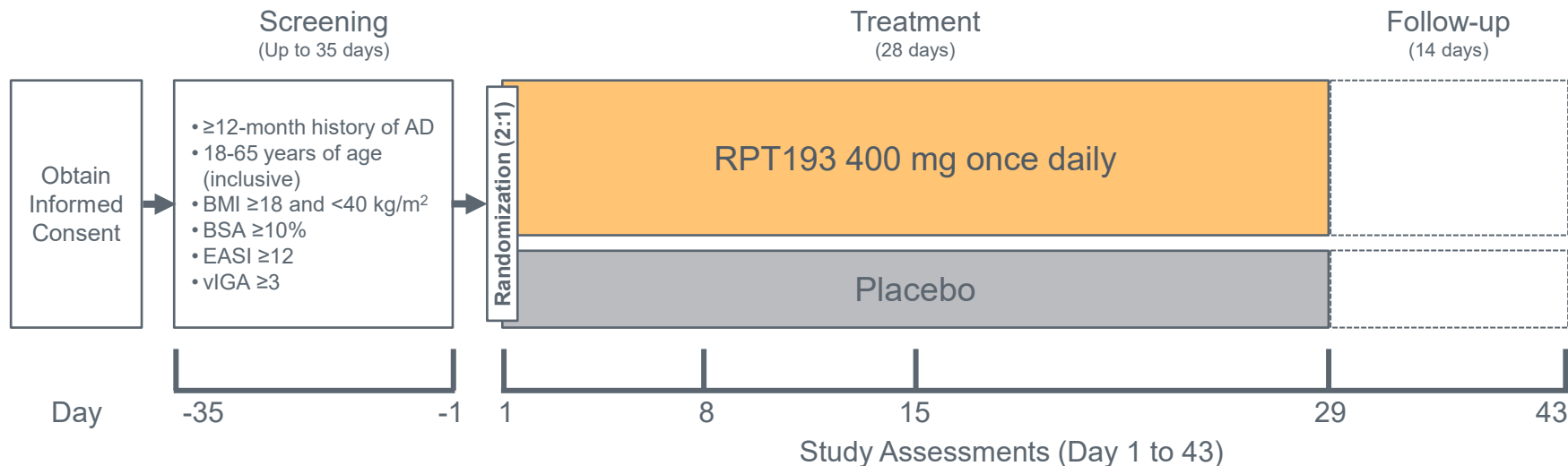
AD Lesional Skin



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



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



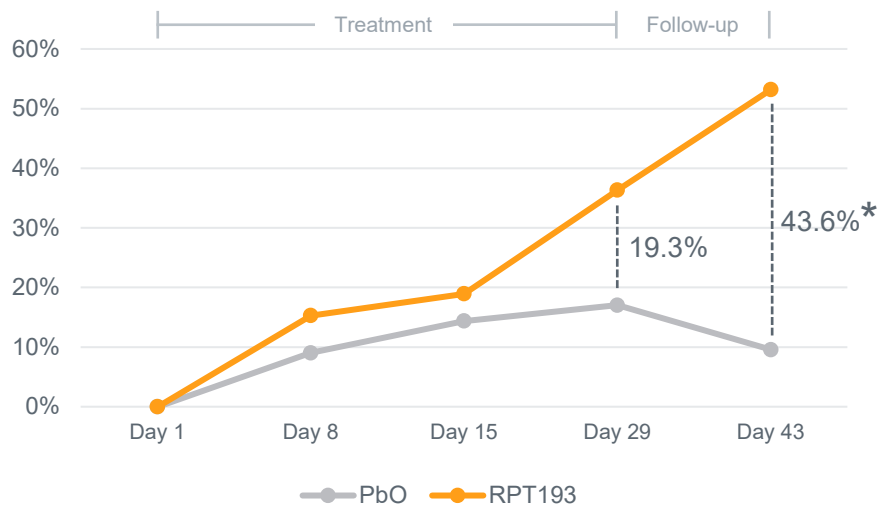
- Enrolled 31 patients into a double-blind, randomized trial with 2:1 allocation of RPT193 to placebo
- Monotherapy study: steroid and immunosuppressant washout period; rescue steroids not permitted through Day 43
- Not powered for any specific endpoint
- Exploratory endpoints include: EASI, Pruritus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

Phase 1b Baseline Demographics and Disease Characteristics

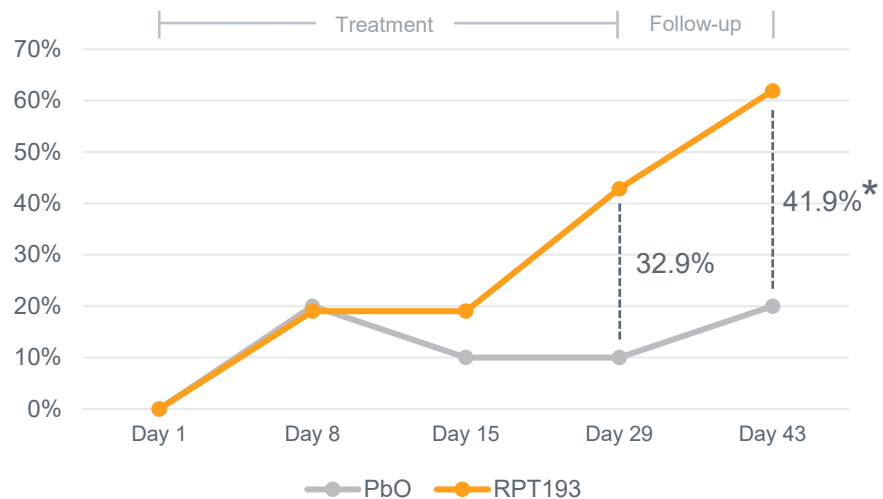
	Placebo	RPT193
N	10	21
Age, Mean (Range)	35.8 (22-64)	41.0 (19-63)
Female, n (%)	4 (40.0%)	12 (57.1%)
Baseline Characteristics		
EASI, Mean (Range)	21.07 (13.6-45.5)	18.49 (12-30)
BSA, Mean (Range)	24.5 (10-61)	23.3 (11-55)
vIGA 3, n (%)	8 (80.0%)	18 (85.7%)
Peak NRS, Mean (Range)	7.3 (3-10)	6.9 (3-10)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



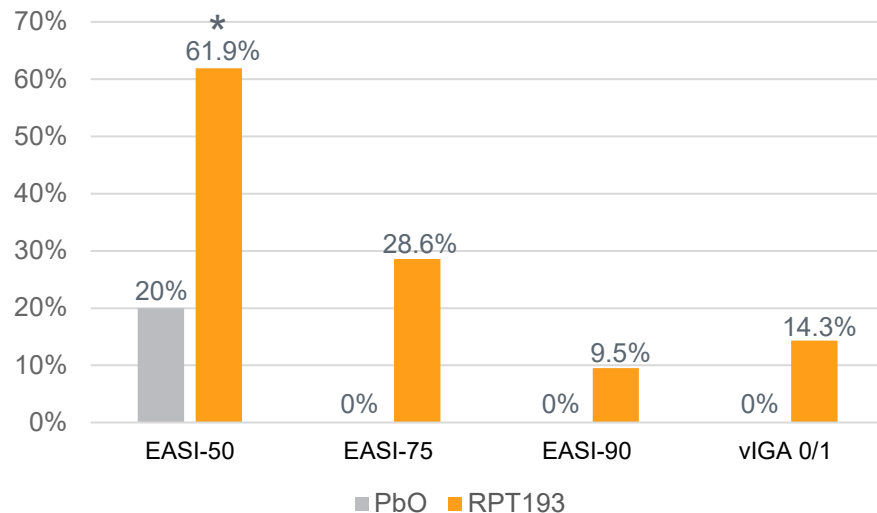
Proportion of EASI-50



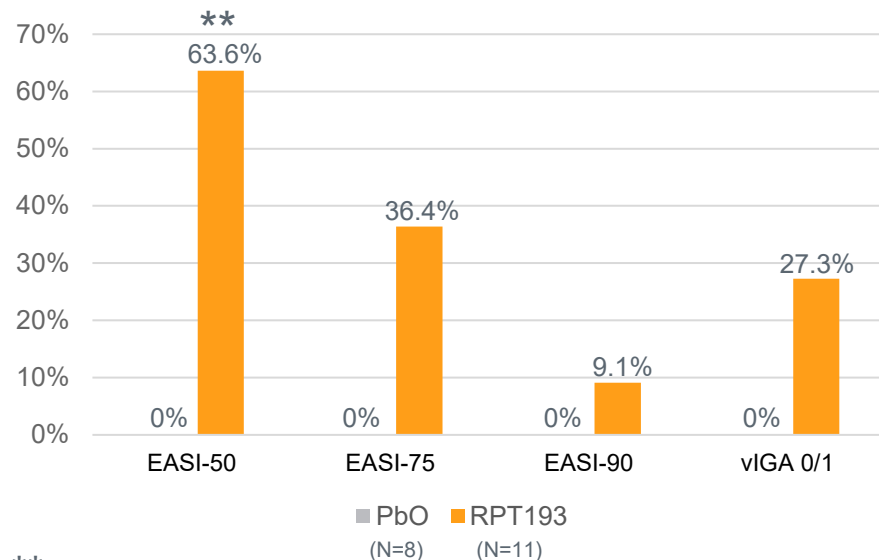
*p < 0.05

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

EASI \geq 12 ITT



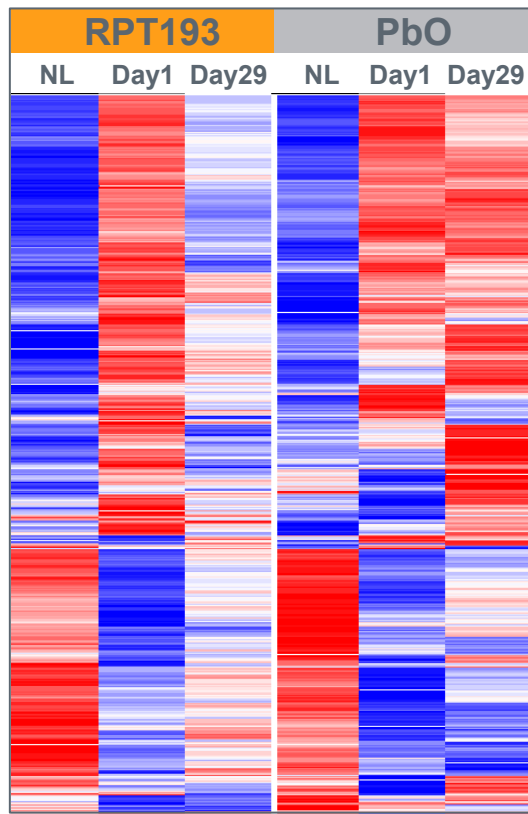
EASI \geq 16 Subgroup



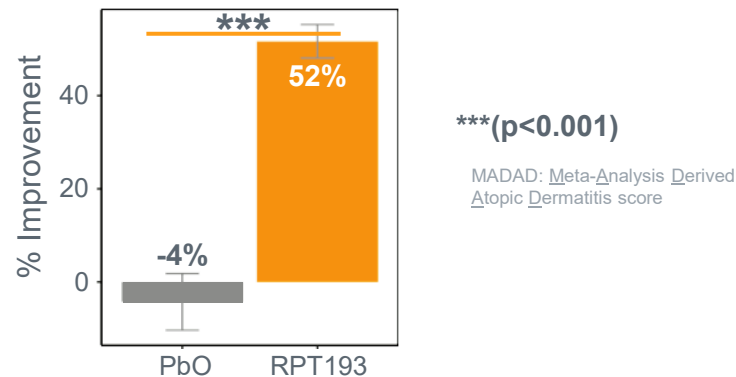
* $p < 0.05$ ** $p < 0.01$

- Similar efficacy between ITT and EASI \geq 16 Subgroup

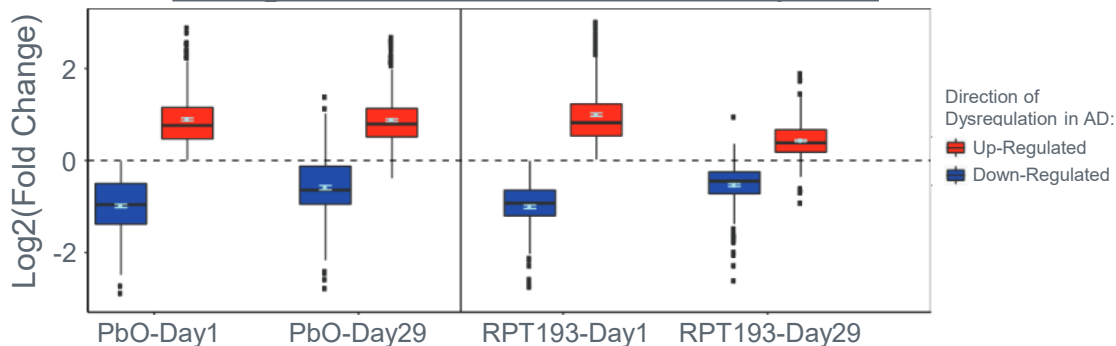
RPT193 Demonstrated Significant Improvement in AD-Associated Gene Signatures in the Skin



Mean % Improvement in MADAD Transcriptome

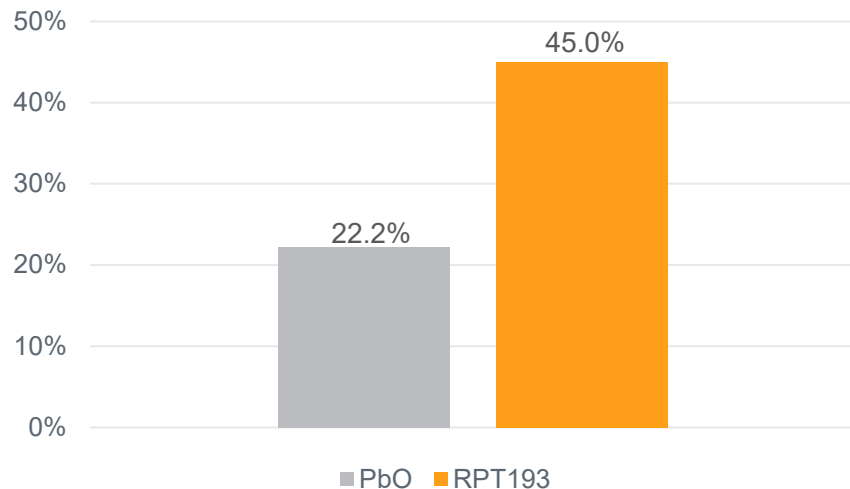


Changes in the Lesional AD Transcriptome

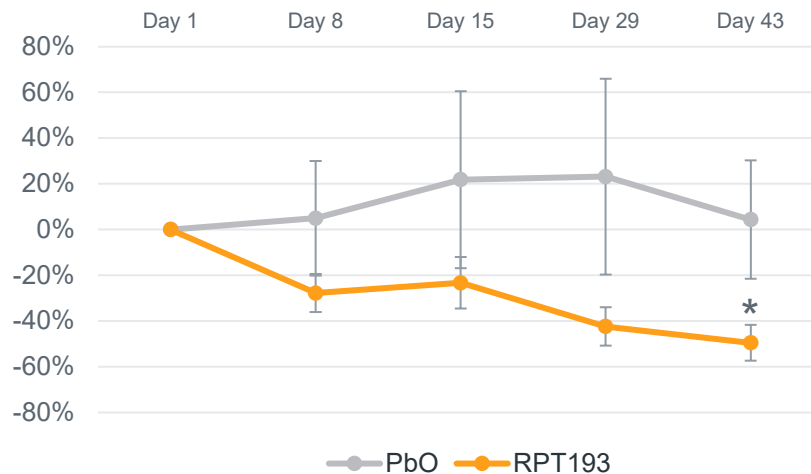


RPT193 Demonstrated Improvement in Itch and Sleep

Proportion of NRS-4[†]



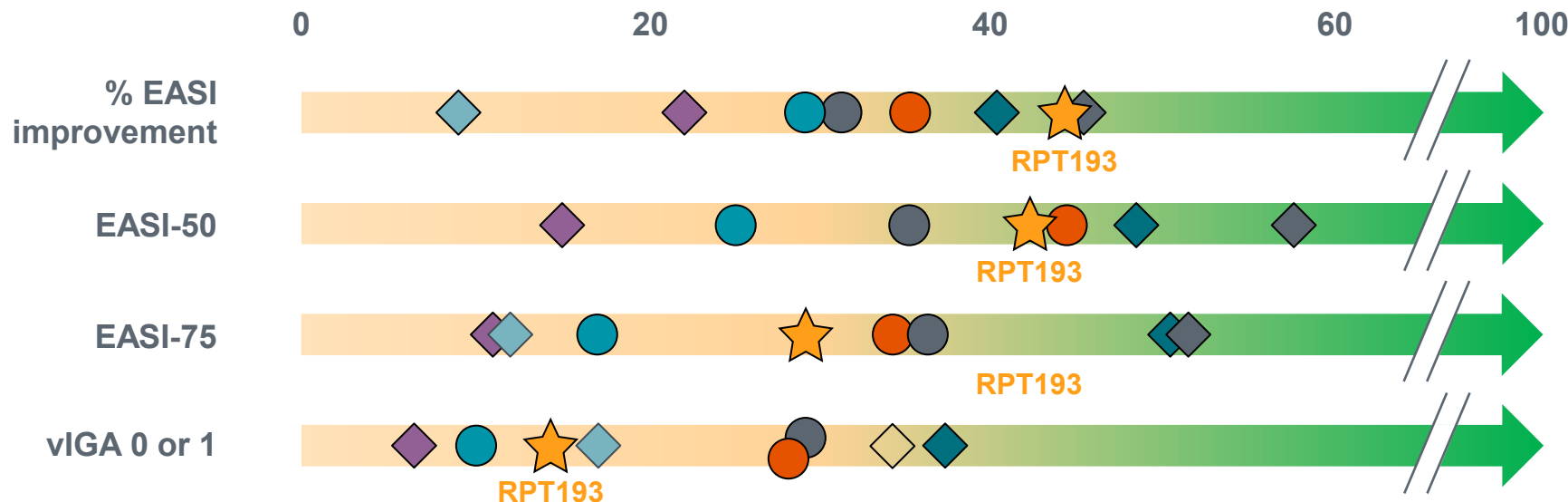
% Change in Patient Oriented SCORAD
(Sleep Loss + Pruritus)



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

* $p < 0.05$

RPT193 6-Week Efficacy vs. 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)

Biologics

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

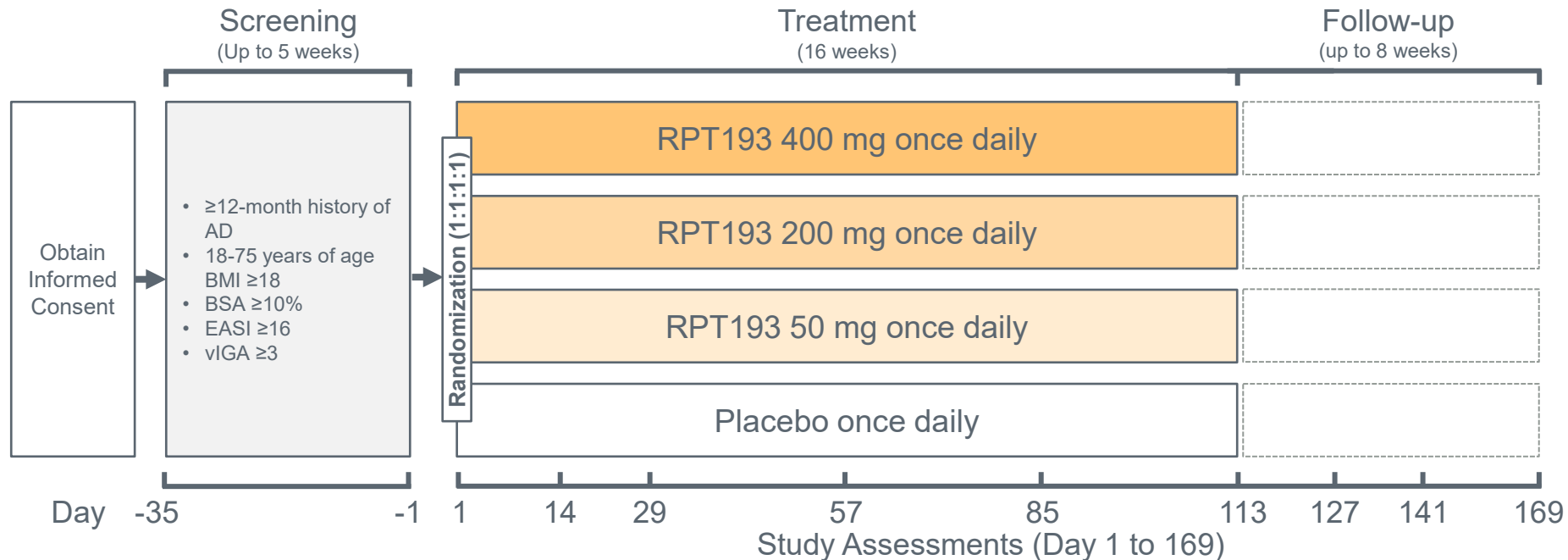
Orals

* 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

RPT193 Phase 1b Safety

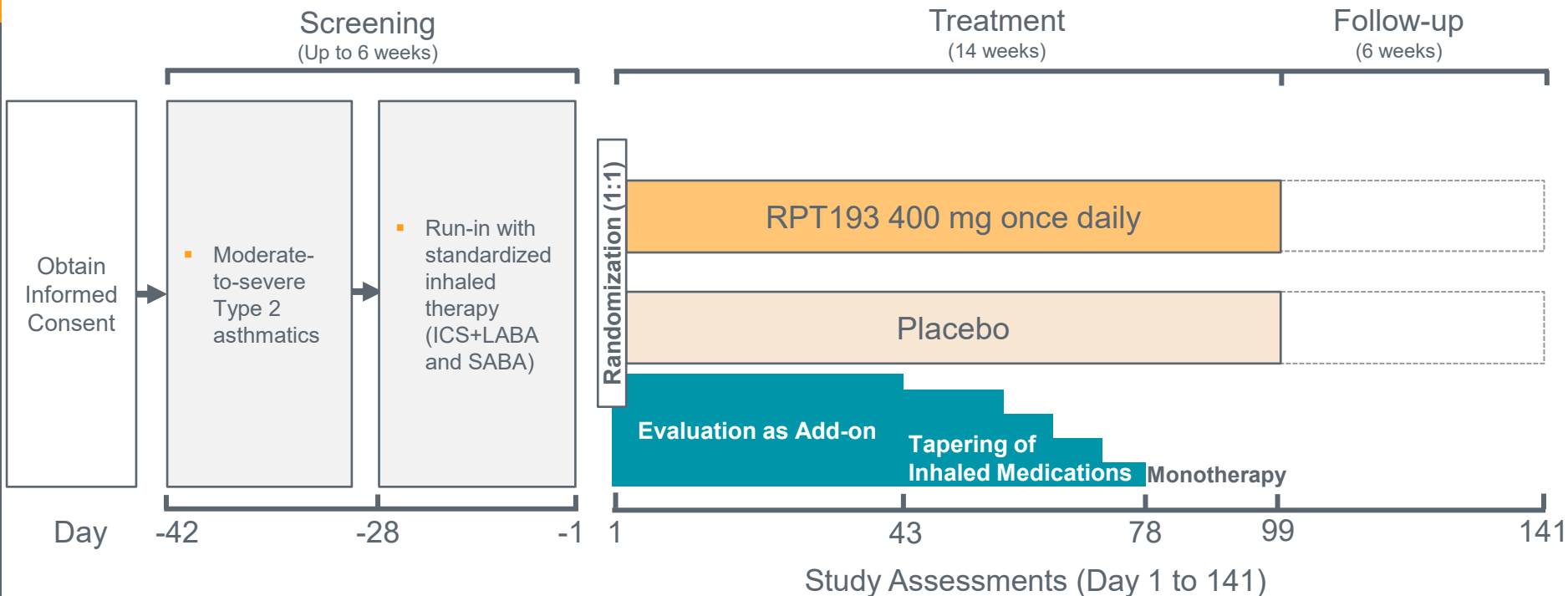
- No SAEs reported
- All AEs reported were mild or moderate in intensity
- No clinically significant safety laboratory abnormalities observed
- Overall safety profile suggests a well-tolerated oral drug that should not require laboratory safety monitoring

Ongoing Dose-Finding Phase 2b Monotherapy Trial in Patients with Moderate-to-Severe Atopic Dermatitis



- **Goal enrollment:** 268 patients, ~67 per arm
- **Monotherapy study:** standard protocol to washout steroids/immunosuppressants and restrict rescue medications
- **Primary endpoint:** EASI
- **Secondary endpoints:** EASI-50/75/90, vIGA, Pruritus NRS

Proposed Phase 2a Asthma Trial Design



- **Goal enrollment:** ~100 patients, ~50 per arm
- **Primary Endpoint:** “Loss of Asthma Control”
- **Secondary Endpoint:** ACQ-5, FEV1, etc.

RPT193 Commercial Vision: Building a Global Blockbuster



Value Statement

Simple, once-daily oral providing symptom relief and lesion reduction
Favorable tolerability and safety from exquisite selectivity



Positioning

As the first-choice systemic therapy



RPT193



Injectable Biologics



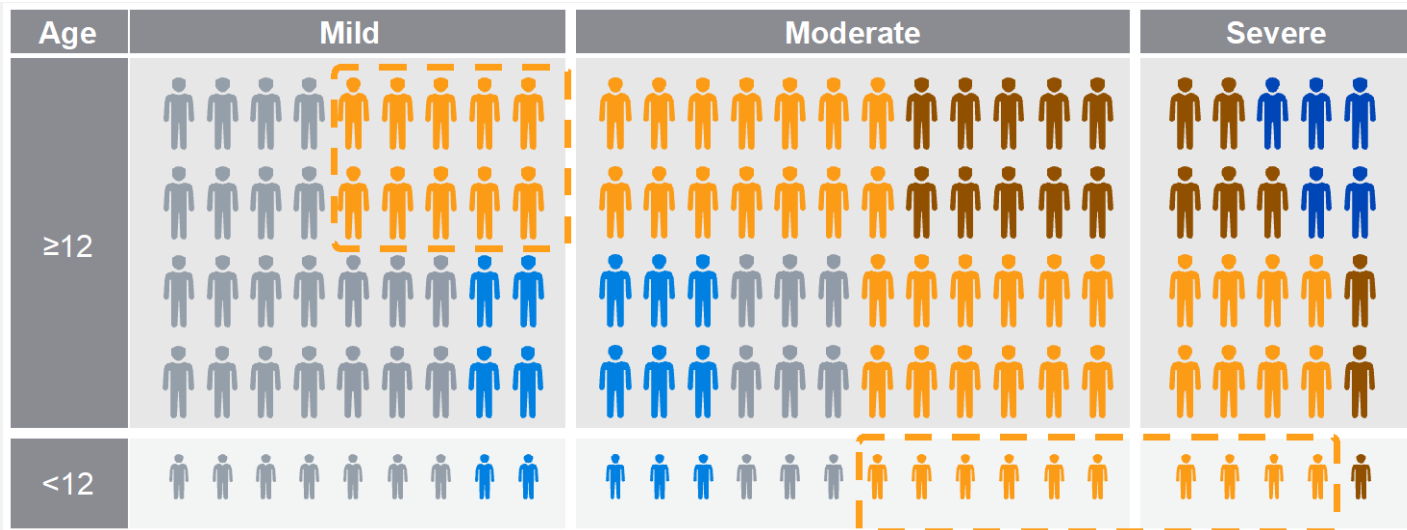
Oral JAKs



Topical JAKs/PDE4



TCS/TCI



LAUNCH

Massive Opportunity
in the \$24B projected
global AD market*

- In Adults and Adolescents ≥ 12 yrs. with Mod-Severe AD



GROW and EXPAND

- In Children <12 yrs. with Mod-Severe AD
- In Adults with Mild AD
- Into the \$21B Asthma Market*
- Additional Th2 Indications

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

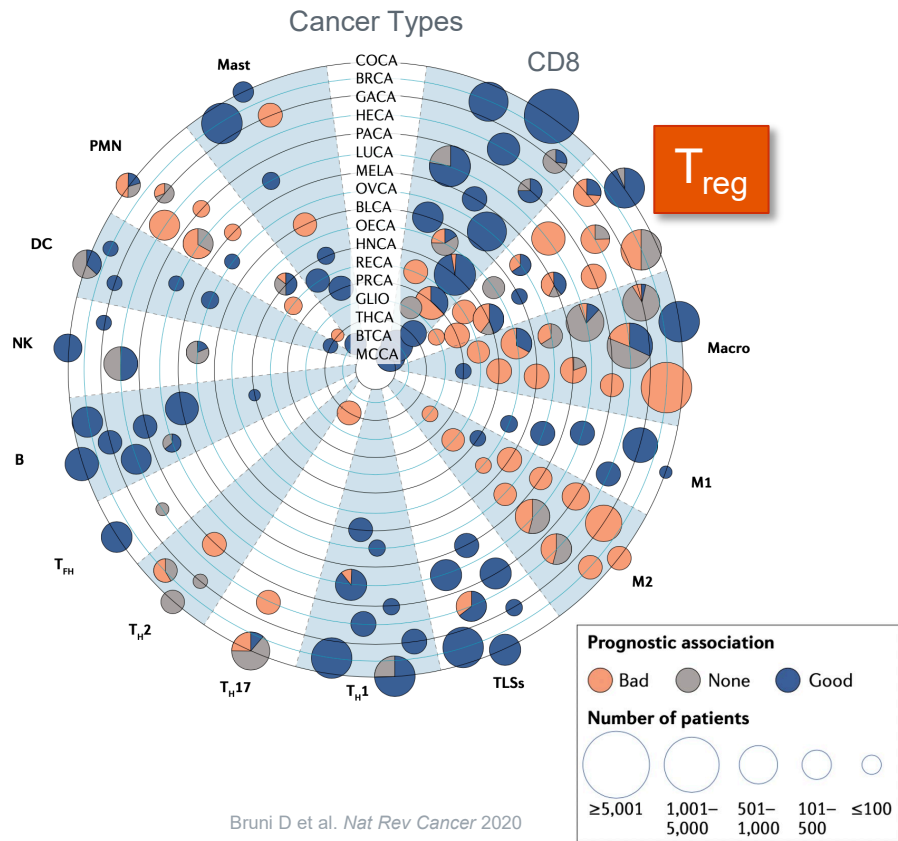
- Oral selective Th2 inhibitor with clear benefit on signs and symptoms in AD
- Well tolerated with favorable safety
- Profile supports competitive positioning ahead of injectables and oral JAKs
- Massive commercial opportunity in AD, asthma and other Th2 indications
- 16-week Phase 2b study in AD ongoing, topline data expected Q4 2023
 - Biologic-like efficacy not required for commercial success
- Plan to initiate Phase 2a study in asthma Q1 2023



FLX475: CCR4 Antagonist for Oncology

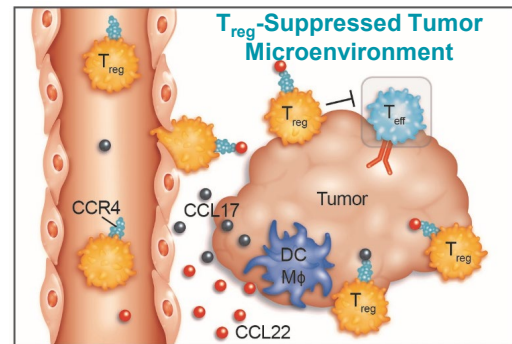
T_{reg} Are Key Targets in the Tumor Microenvironment (TME)

- 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

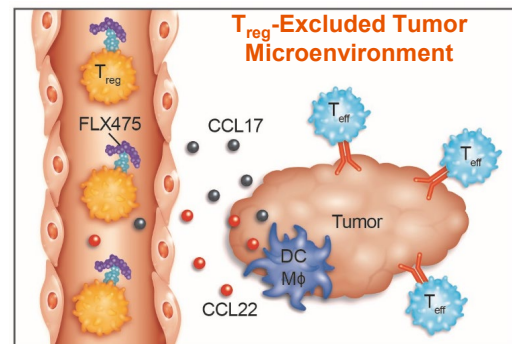


FLX475: Tumor Specific T_{reg} Inhibitor in Phase 2

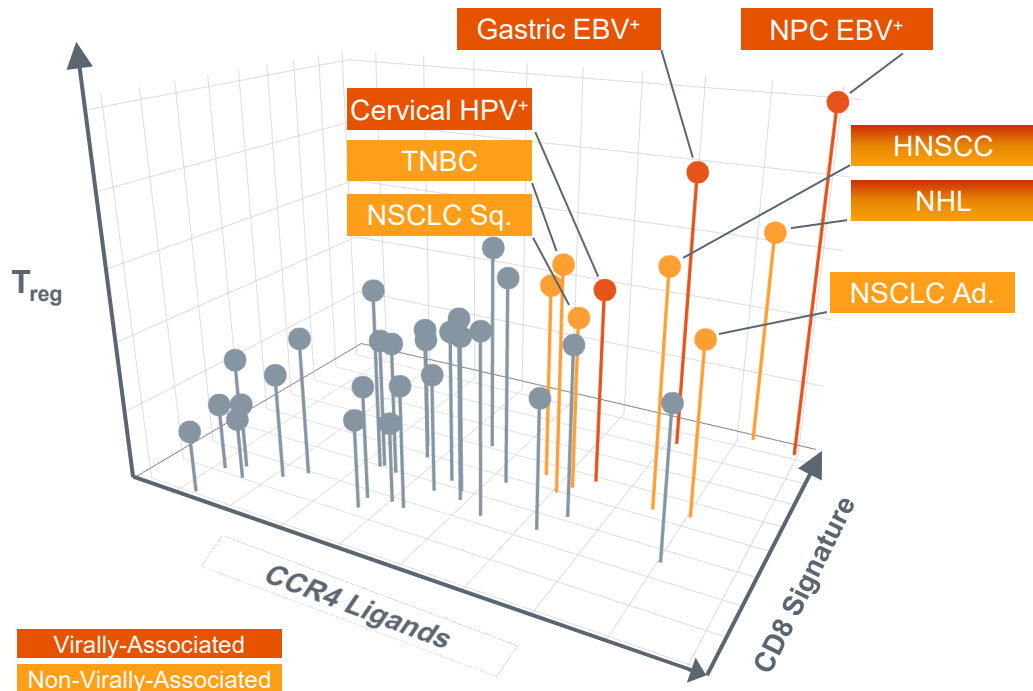
- **Chemically distinct** potent and selective CCR4 small molecule antagonist
- **Selectively blocks tumor T_{reg}** while sparing normal tissues and beneficial cells
- **Potential for superior safety and efficacy** compared to depleting antibodies
- **US patent coverage through 2037**
- **Monotherapy and combination antitumor activity** in charged cancers



FLX475



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

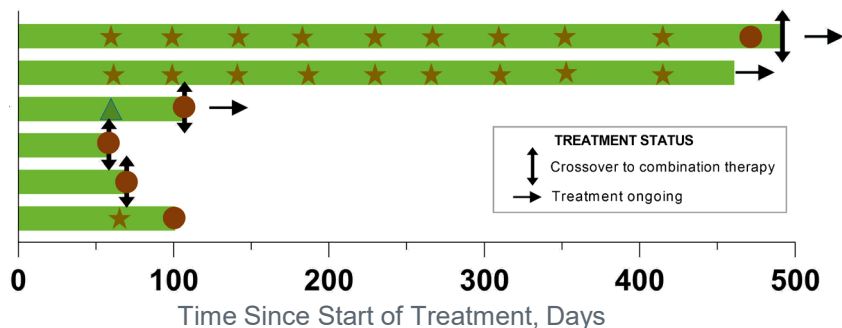
Non-Hodgkin Lymphoma; NSCLC Non-Small Cell Lung Cancer; TNBC Triple

Negative Breast Cancer

- “Charged” tumors: high CCR4 ligands, T_{reg} and CD8 T cells
- Potential for both monotherapy and combination activity
- Include cancers with high unmet need and large markets
- Phase 2 trial expansions focused on charged cancers

Encouraging Monotherapy and Combination Efficacy

EBV+ NK/T Lymphoma (Monotherapy)

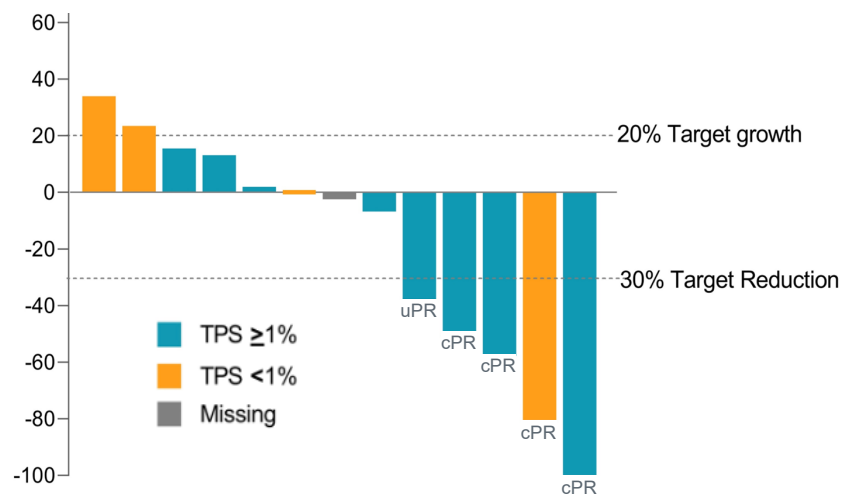


PET-CT-BASED RESPONSES: ★ Complete metabolic response ▲ Partial metabolic response ● Progressive metabolic disease

- 4 of 6 responses to FLX475 monotherapy including 2 confirmed durable CMR

- Design:** Open-label Phase 2, Simon 2-Stage Design
- Indications:** Charged tumors with ≥ 1 line of therapy
- Dose:** FLX475 100 mg QD; pembro 200 mg Q3wk

CPI-Naïve NSCLC (Combo)



ORR Comparison in PD-L1+* NSCLC

Pembro Mono	Pembro+TIGIT	Pembro+FLX475
18% [†]	31% (4/13) [^]	38% (3/8)

*TPS $\geq 1\%$; [†]Keynote-010; [^]Niu et al. ESMO 2020

FLX475 Program Summary

- Highly selective tumor T_{reg} inhibitor differentiated from biologics
- Encouraging early efficacy as monotherapy and in combination with pembrolizumab
- Favorable safety and convenient oral dosing support broad combinability
- Enrolling Stage 2 expansions in 3 indications including CPI-naïve NSCLC
 - Partner Hanmi Pharmaceuticals is testing FLX475 + pembro in gastric cancer
- Data update expected in 2H 2023

Key Takeaways and Upcoming Milestones

- **RPT193**: safe oral agent designed for a broad range of inflammatory diseases, in a definitive Phase 2b study in AD
- **FLX475**: highly selective tumor T_{reg} inhibitor in multiple Phase 2 expansions as monotherapy and in combination with pembrolizumab
- **Planned Key Milestones**
 - **Q1 2023**: RPT193 Phase 2a asthma trial start
 - **Q4 2023**: RPT193 Phase 2b AD topline data
 - **2H 2023**: FLX475 Phase 2 data update



Thank You

