



Transforming the Treatment of Inflammation and Cancer

January 2024
Corporate Presentation

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Novel Oral Drugs That Target Critical Immune Drivers

- Proprietary discovery engine
- Clinically de-risked assets
- Large market opportunities
- Strategic collaborations
- Strong cash position

CLINICAL

Zelnecirnon (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 mid 2024
- Phase 2a in Asthma ongoing

Tivumecirnon (Oncology): MERCK

- Selectively targets immunosuppressive tumor T_{reg}
- PoC in Phase 2 with mono and combo efficacy
- 45% ORR* as PD-1 combo in CPI-naïve NSCLC

DISCOVERY

Additional inflammation and oncology targets

*Trial ongoing and data could mature

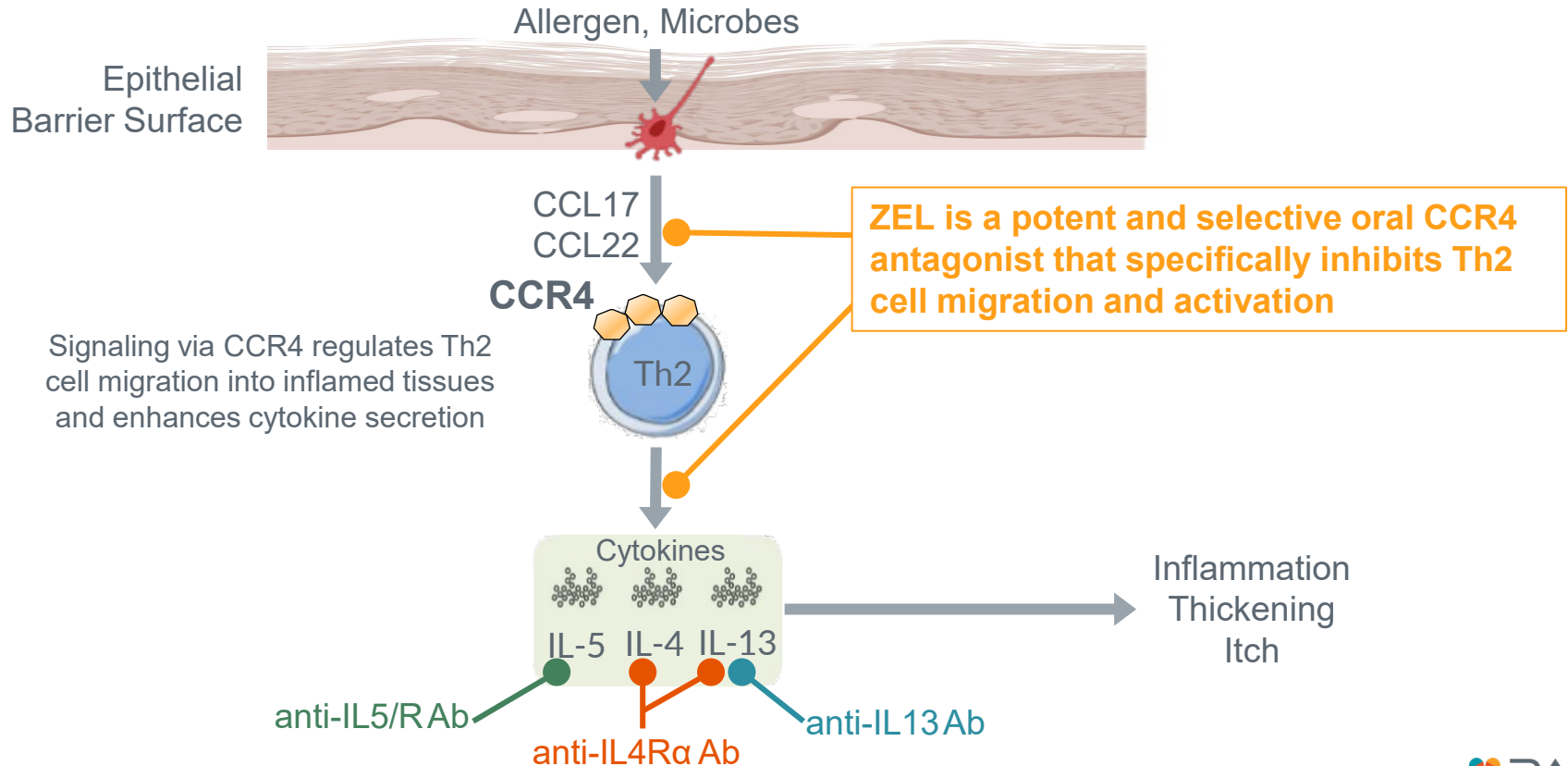


Zelnecirnon (RPT193): CCR4 Antagonist for Inflammatory Diseases

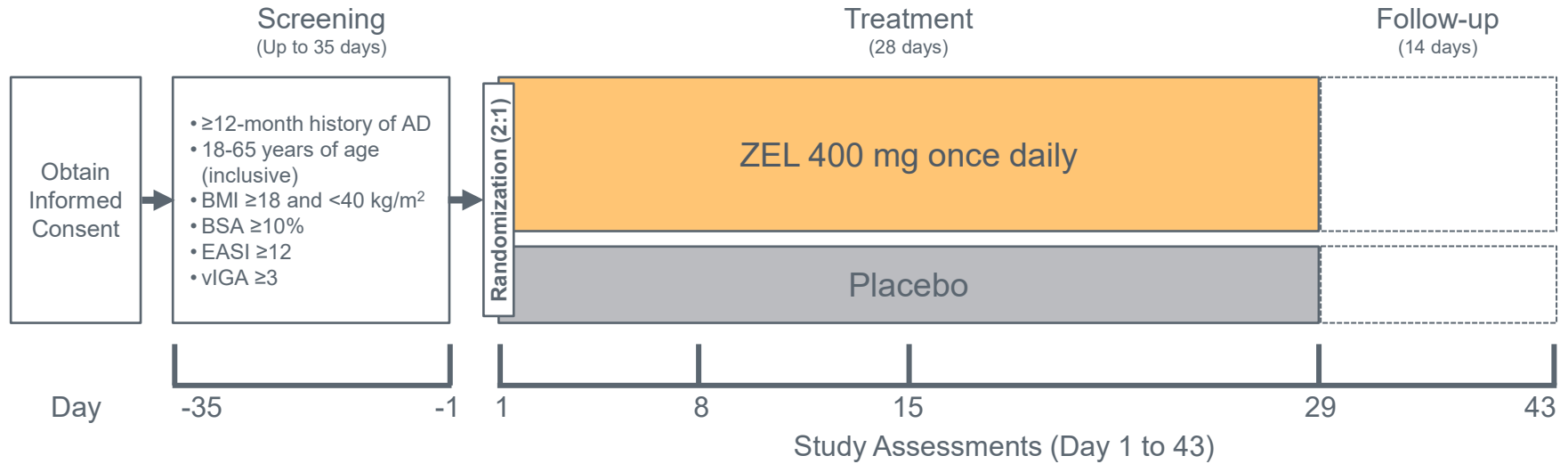
Zelnecirnon: First-in-Class Oral Th2 Inhibitor for Inflammatory Diseases

- **Highly potent and selective once-daily oral** CCR4 antagonist designed to safely reduce Th2-inflammation
- **Clear benefit on signs and symptoms as monotherapy** in a 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, prior to injectables and JAKs
- **Phase 2b AD data expected mid 2024**, pivotal studies anticipated in 2025
- **Phase 2a asthma trial ongoing**
- **Pipeline in a Product:** potential in many Th2 disorders

Zelnecirnon Targets Th2 Cells, Key Drivers of Inflammation in AD, Asthma and Other Diseases



Phase 1b Trial Explored Zelnecirnon Safety and Efficacy in Patients with Moderate-to-Severe Atopic Dermatitis



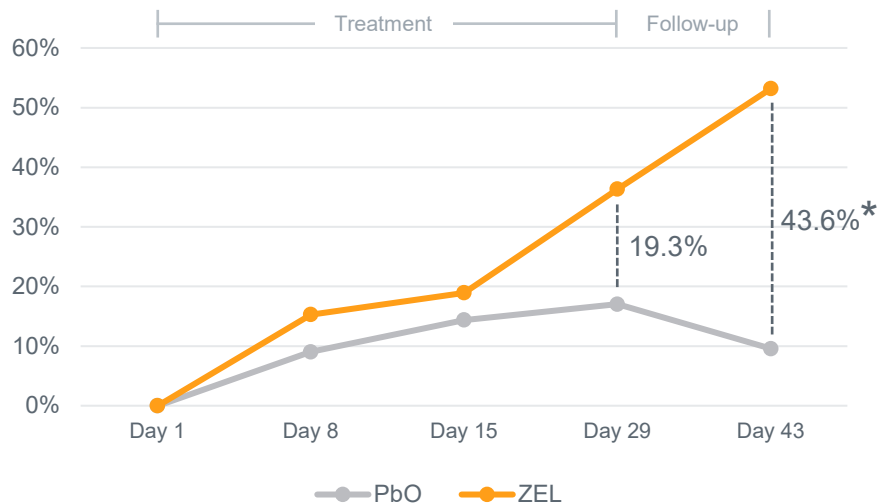
- Enrolled 31 patients into a double-blind, randomized trial with 2:1 allocation of ZEL to placebo
- Monotherapy study: steroid and immunosuppressant washout period; rescue steroids not permitted through Day 43
- Not powered for any specific endpoint
- Exploratory endpoints include: EASI, Pruritus Numerical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

Phase 1b Baseline Demographics and Disease Characteristics

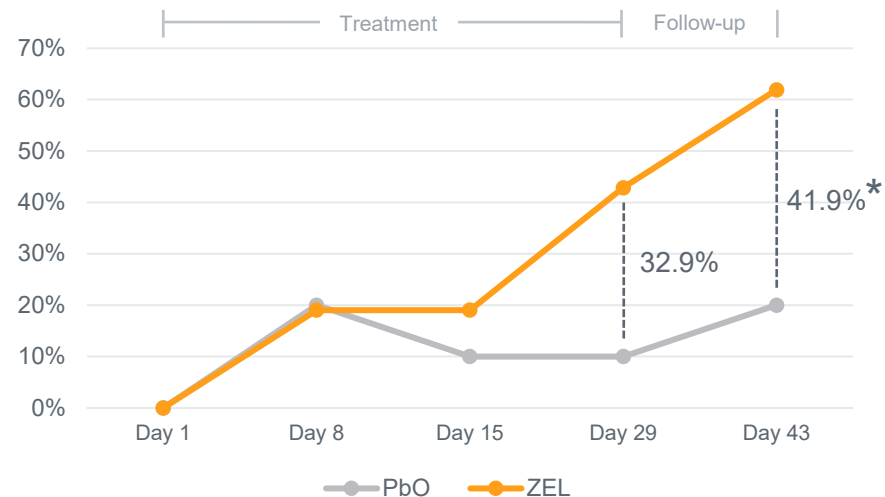
	Placebo	ZEL
N	10	21
Age, Mean (Range)	35.8 (22-64)	41.0 (19-63)
Female, n (%)	4 (40.0%)	12 (57.1%)
Baseline Characteristics		
EASI, Mean (Range)	21.07 (13.6-45.5)	18.49 (12-30)
BSA, Mean (Range)	24.5 (10-61)	23.3 (11-55)
vIGA 3, n (%)	8 (80.0%)	18 (85.7%)
Peak NRS, Mean (Range)	7.3 (3-10)	6.9 (3-10)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

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

% Improvement in EASI



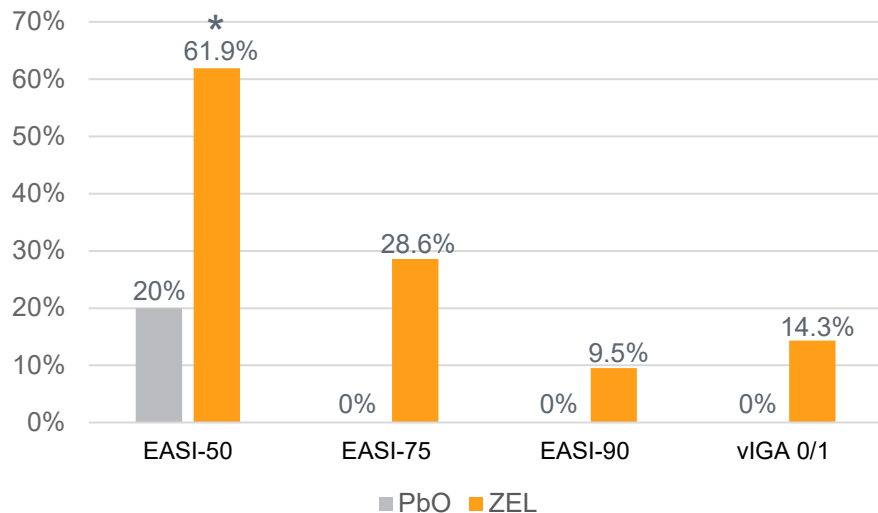
Proportion of EASI-50



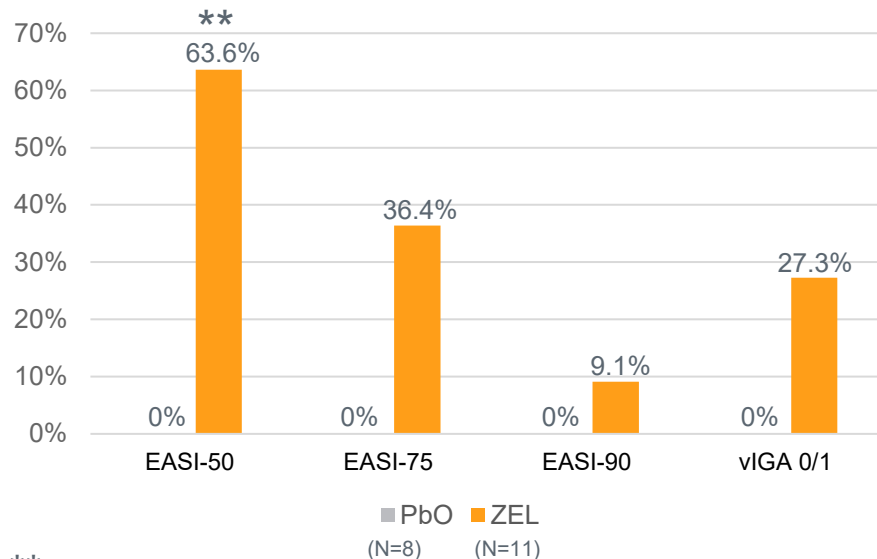
*p < 0.05

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

EASI \geq 12 ITT



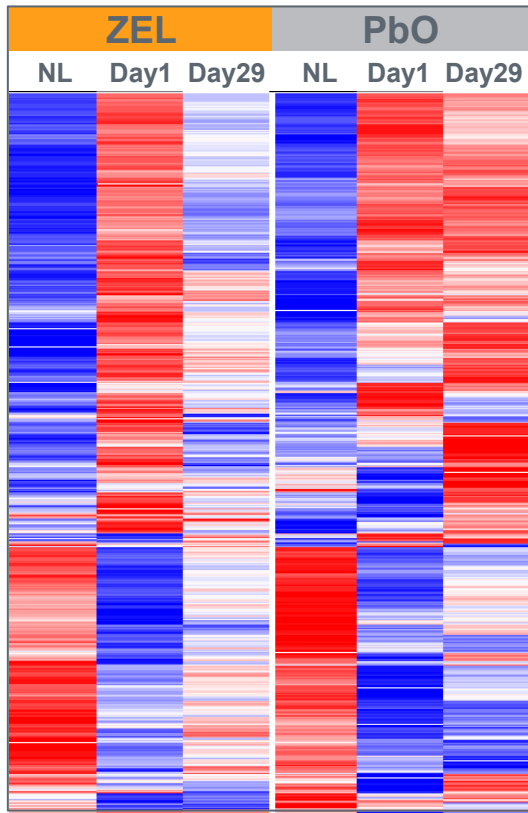
EASI \geq 16 Subgroup



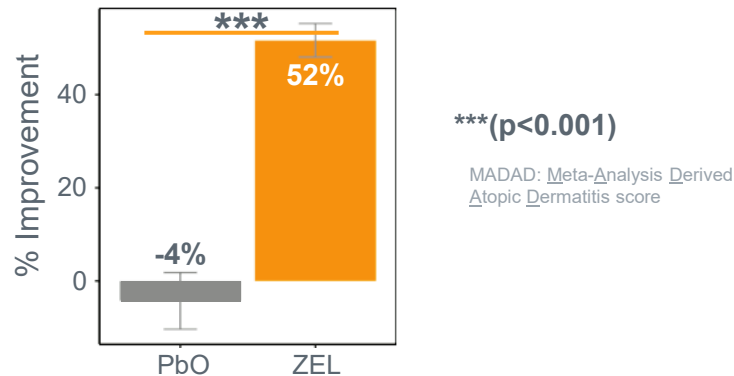
*p < 0.05 **p < 0.01

- Similar efficacy between ITT and EASI \geq 16 Subgroup

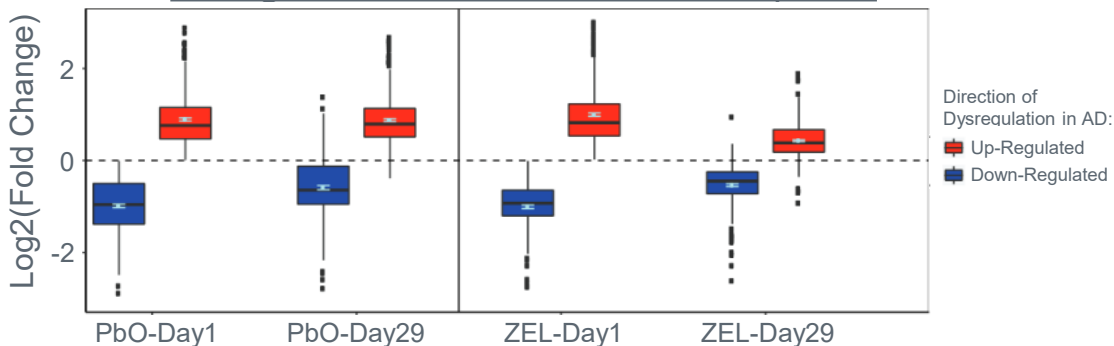
Zelnicirnon Demonstrated Significant Improvement in AD-Associated Gene Signatures in the Skin



Mean % Improvement in MADAD Transcriptome

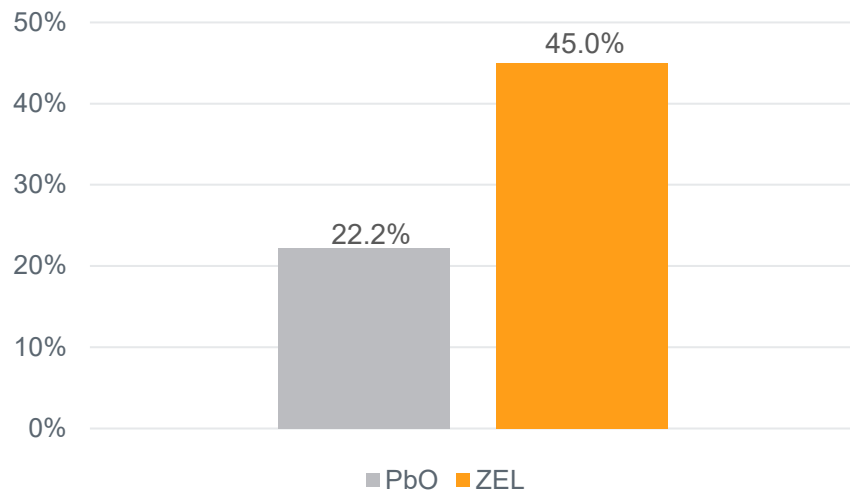


Changes in the Lesional AD Transcriptome

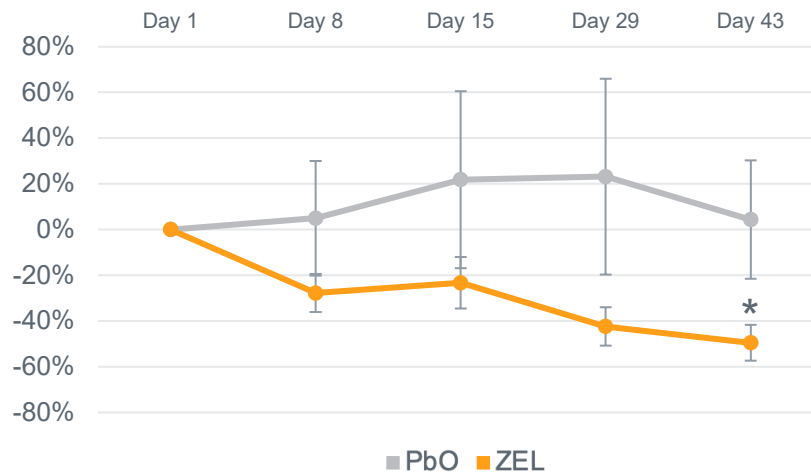


Zelnecirnon Produced Improvement in Itch and Sleep

Proportion of NRS-4[†]



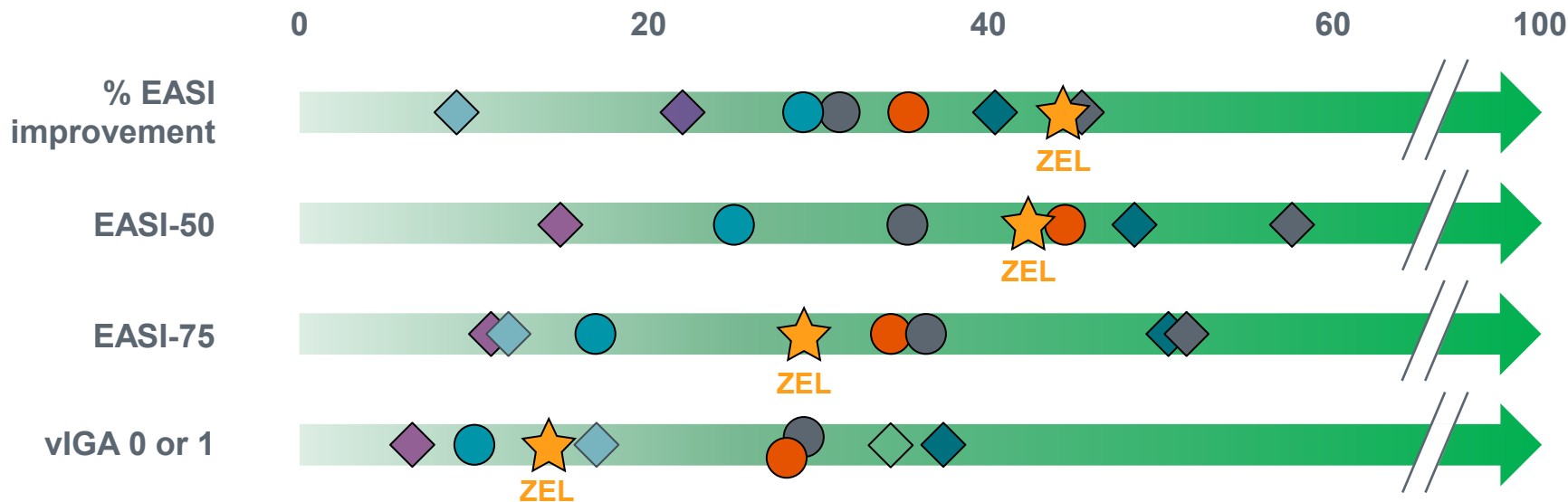
% Change in Patient Oriented SCORAD
(Sleep Loss + Pruritus)



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

* $p < 0.05$

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



All data shown are placebo-adjusted



- | | | | | | | |
|-------------------------------|----------------------------------|----------------------------------|----------------------------|--------------------------|------------------------|------------------------------|
| ● 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

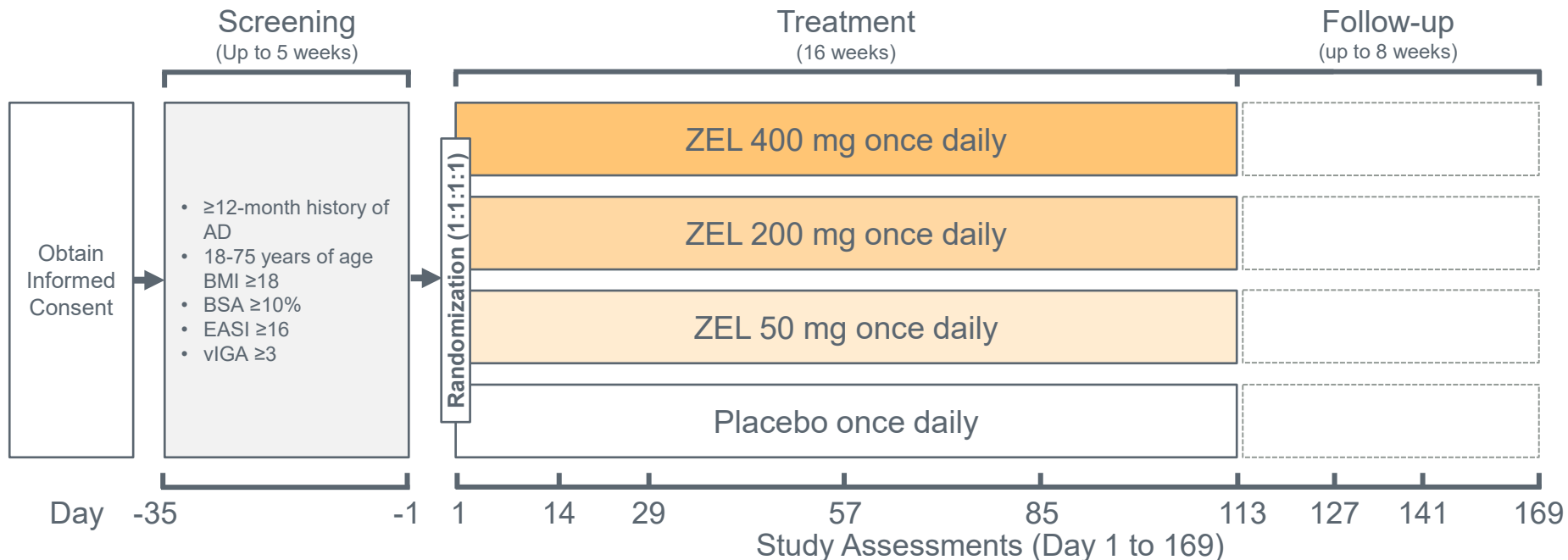
Orals

* 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

Zelnecirnon Phase 1b Safety

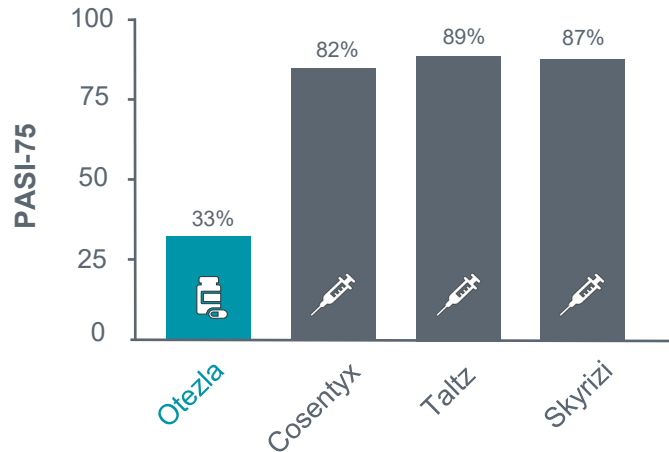
- No SAEs reported
- All AEs reported were mild or moderate in intensity
- No clinically significant safety laboratory abnormalities observed
- Overall safety profile suggests a well-tolerated oral drug that should not require laboratory safety monitoring

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

Otezla* Shows That A Safe Oral Drug With Modest Efficacy Can Be A Commercial Success



- No black box warning
- No laboratory monitoring

Positioning after TCS:
Preferred Option

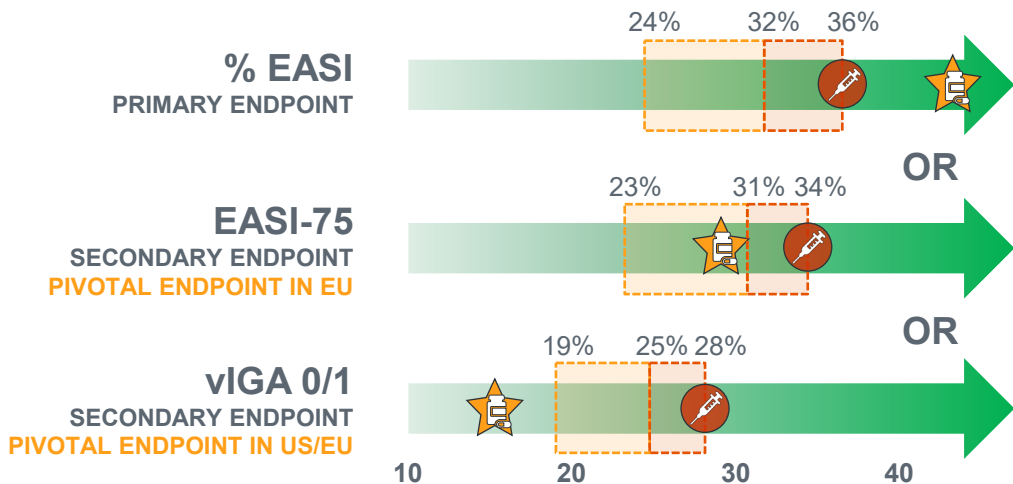
Est. Peak sales:
\$2.6B

Amgen acquisition price:
\$13B

*Otezla® (apremilast) is a registered trademark of Amgen, Inc.

Zelnecirnon Can Be Commercially Successful Across a Broad Range of Efficacy

Zelnecirnon Efficacy Ranges



All data shown are placebo-adjusted

ZEL at 6 wk dupilumab at 16 wk

Efficacy Supporting **≥\$4-6B**
Peak US Revenue in AD

Efficacy Supporting **≥\$6-8B**
Peak US Revenue in AD

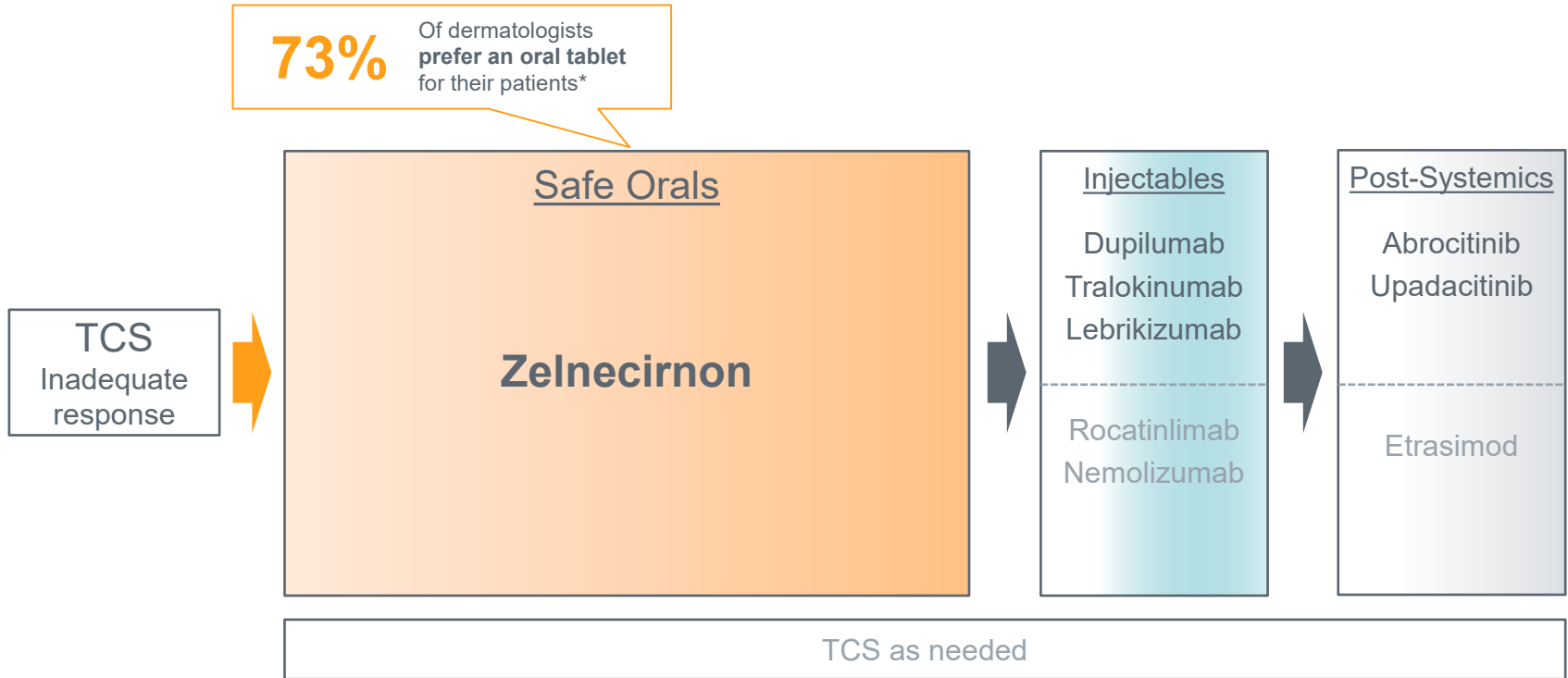
Zelnecirnon Phase 2b Success

- Efficacy in target range ($\geq 2/3$ of dupilumab) and statistically significant on any primary or pivotal endpoint
- Upside: Efficacy similar or greater than dupilumab ($\geq 90\%$ of dupilumab)
- Phase 3 dose(s) identified

Expect Zelnecirnon to Be Positioned as the Preferred First Option After TCS Inadequate Response

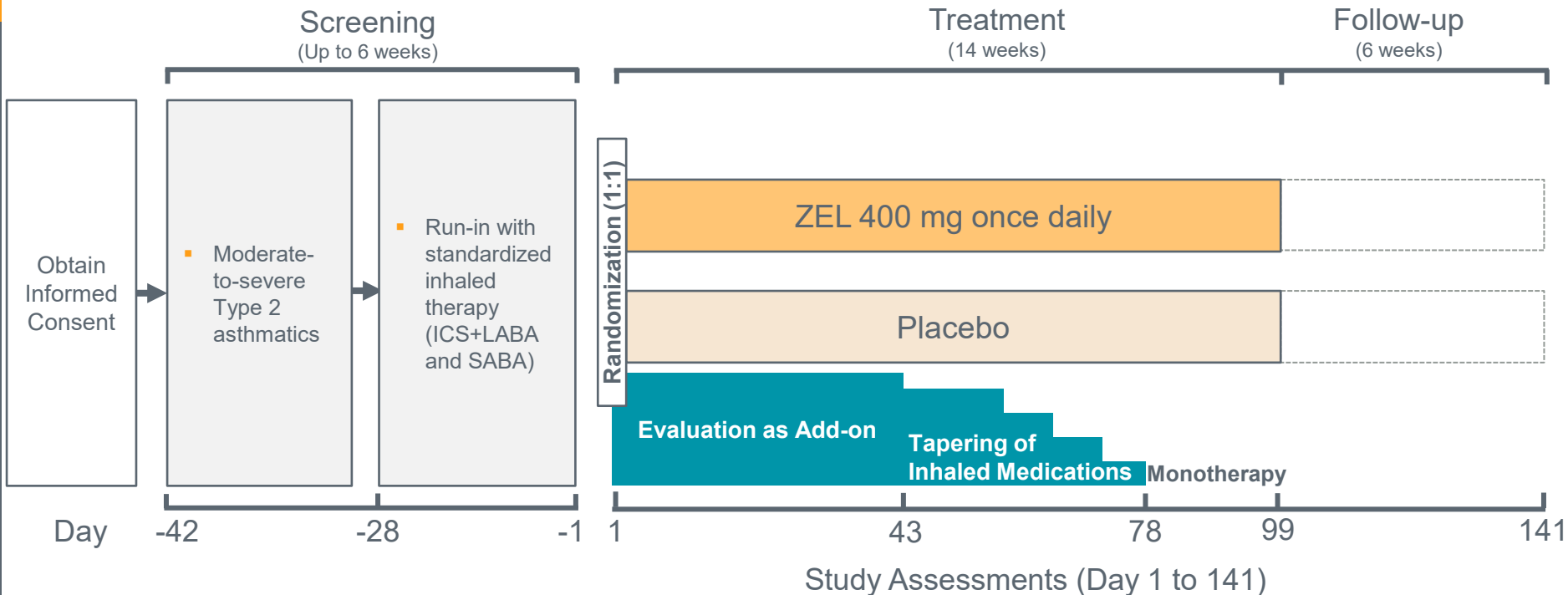
73%

Of dermatologists prefer an oral tablet for their patients*



* RAPT Therapeutics US quantitative market research N=50 US dermatologists

Phase 2a Asthma Trial Design



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

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



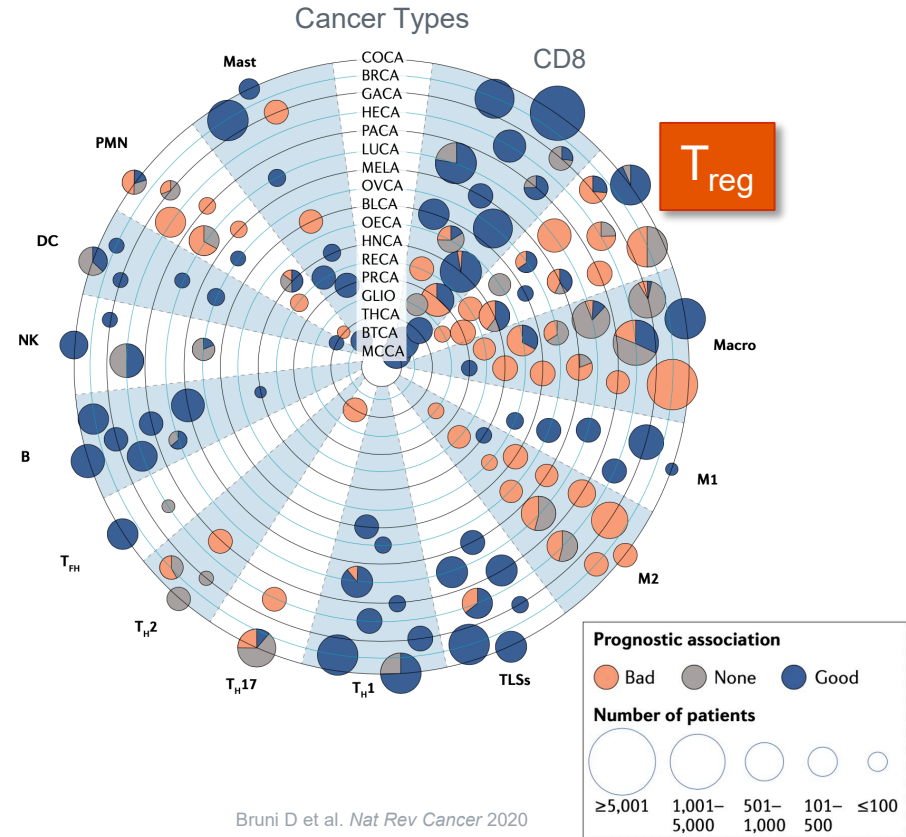
Tivumecirnon (FLX475): CCR4 Antagonist for Oncology

Tivumecirnon: First-in-Class T_{reg} Inhibitor for Cancer

- **Oral CCR4 antagonist selectively inhibits tumor T_{reg} trafficking**
- **Positive TIVU/anti-PD-1 efficacy** in PD-L1+ CPI-naïve NSCLC
 - 45% confirmed ORR: numerically superior to anti-PD-1 and TIGIT/anti-PD-1
 - Differentiated efficacy in “cool” PD-L1 low tumors
 - Initial PFS 6.3 months; data continuing to mature
- **Positive tivumecirnon/anti-PD-1 efficacy** in EBV+ gastric cancer (Hanmi)
- **Monotherapy efficacy**: deep responses in NK/T cell lymphoma and beneficial biomarker changes in solid tumors
- **Favorable safety profile** in >300 patients support broad combinability

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

- Potent suppressors of effector T cells and antigen presenting cells
- 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} specifically in the tumor



Tivumecirnon's Advantage: Selective Inhibition of Tumor T_{reg}

Traditional Approach:
Depleting Antibodies



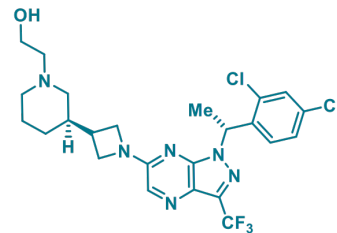
Examples: anti-CD25,
anti-CCR4, anti-CCR8

ADCC-mediated T_{reg} depletion

POTENTIAL ISSUES

- ! Systemic depletion of T_{reg}
= **increases toxicity**
- ! Poor/variable T_{reg} depletion in the
tumor = **reduces efficacy**
- ! Nonspecific depletion of antitumor
T cells = **reduces efficacy**

RAPT's Solution:
Tivumecirnon



Blocks **tumor-specific** T_{reg} trafficking

ADVANTAGES

- + Specific reduction of tumor T_{reg}
= **reduces toxicity**
- + Robust reduction of tumor T_{reg}
= **increases efficacy**
- + No depletion of anti-tumor T cells
= **increases efficacy**

Tivumecirnon Phase 2 Clinical Development

Phase 2 Stage 1 (N≥10)

Phase 2 Stage 2 (N≥19)

T_{reg}⁻ and CCR4 ligand-enriched tumors selected for individual trial cohorts

Monotherapy

Monotherapy

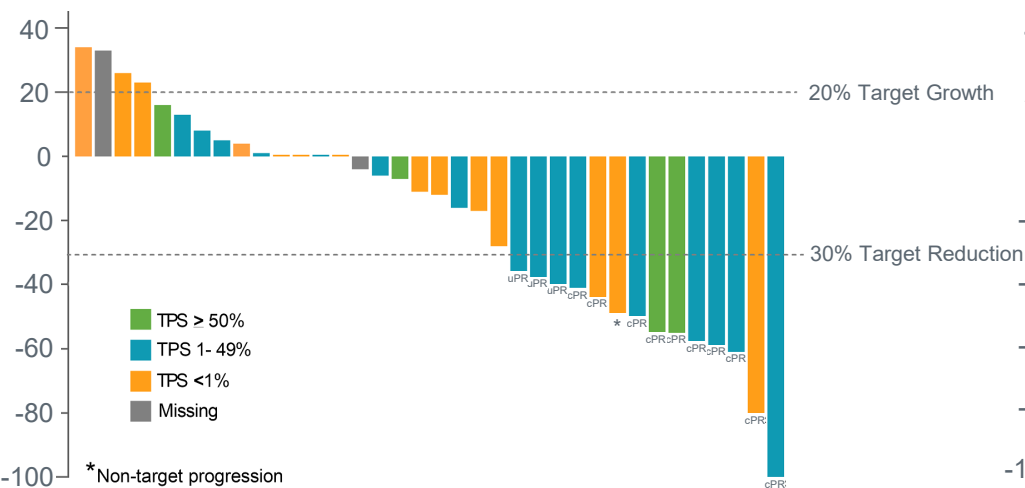
Combination w/
pembrolizumab

Combination w/
pembrolizumab

- **Design:** Open-label Phase 2, Simon 2-Stage Design
- **Doses:** TIVU 100 mg QD; pembrolizumab 200 mg Q3 wk
- **Endpoints:** Safety, PK, Biomarkers, Objective Response Rate

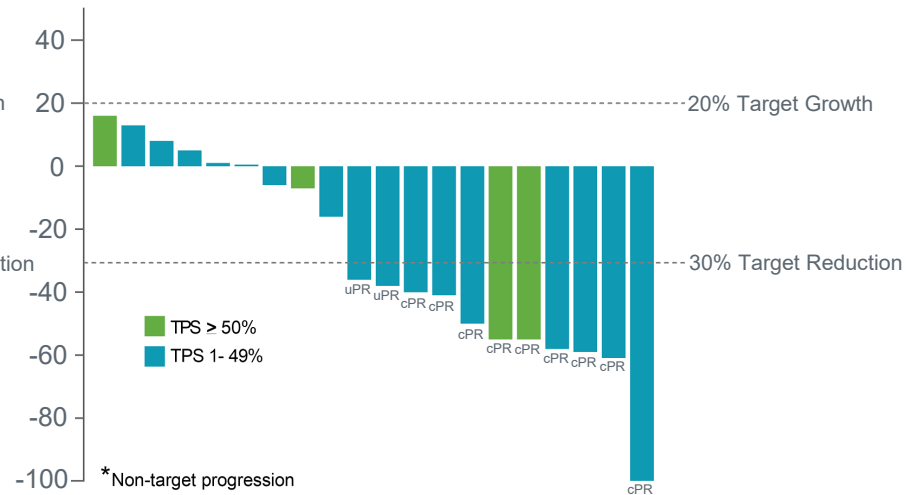
Positive Phase 2 Clinical Efficacy in CPI-Naïve NSCLC Presented at SITC 2023

BOR All Evaluable (n=36)



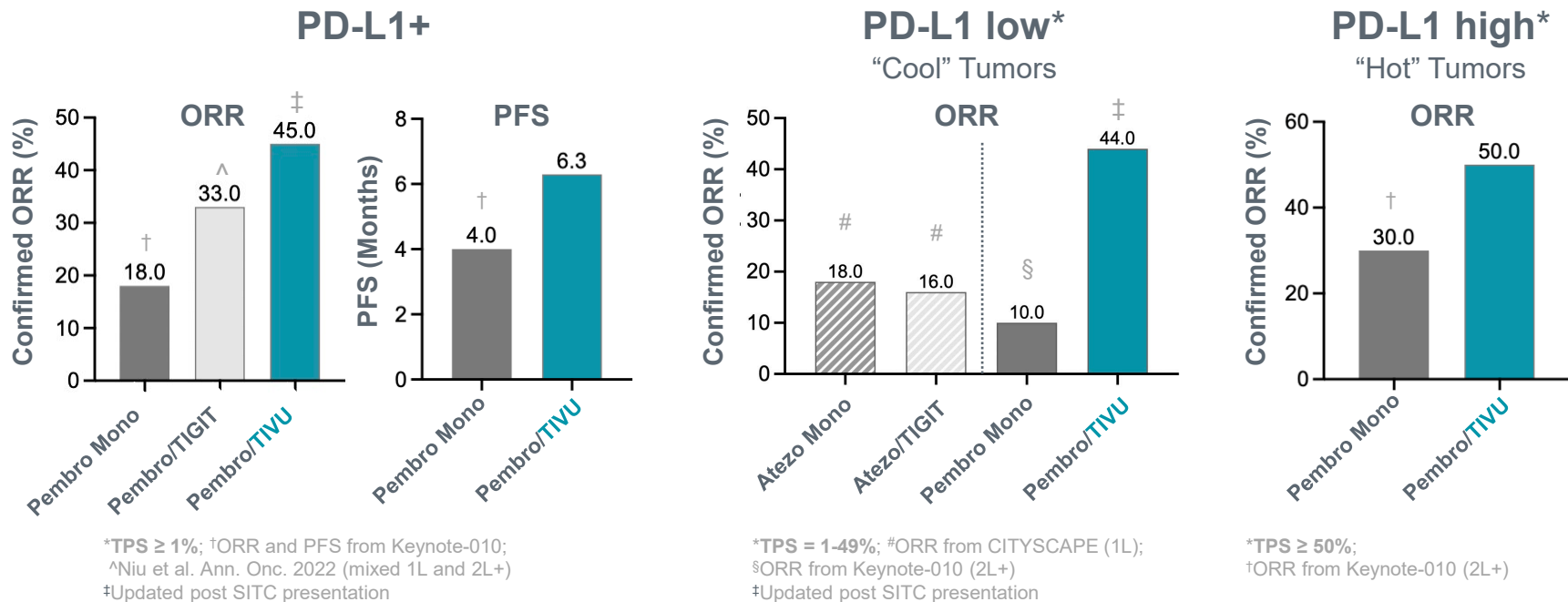
- Overall confirmed ORR: 31% (11/36), regardless of PD-L1 status
- Post SITC: additional PR confirmed

BOR PD-L1+ (n=20)



- PD-L1+ confirmed ORR = 45% (9/20)**
 - Post-SITC: additional PR confirmed
- PD-L1+ median PFS = 6.3 mo.**
- Data expected to mature/improve**

Historical Context for Promising Tivumecirnon/Pembro Efficacy in CPI-naïve NSCLC



Cross trial comparisons; Data do not represent randomized comparisons

Large Commercial Opportunities in 1L NSCLC

Line of Therapy	Combination	NSCLC Segment	US Market Size
1L	PD-(L)1/TIVU	PD-L1 high (TPS \geq 50%)	27,300
	PD-(L)1/TIVU/Chemo	All PD-L1 (TPS = 0-100%)	106,000
	PD-(L)1/TIVU/TIGIT	PD-L1 high (TPS \geq 50%)	27,300

Key Takeaways and Upcoming Milestones

- **Zelnecirnon**: first-in-class safe oral designed to be the preferred option across a range of inflammatory diseases, now in a Phase 2b study in AD and a Phase 2a study in asthma
- **Tivumecirnon**: first-in-class selective tumor T_{reg} inhibitor with monotherapy efficacy and encouraging PD-1 combo efficacy in CPI-naïve NSCLC
- **Planned Key Milestone**
 - **mid 2024**: Zelnecirnon Phase 2b AD topline data



Thank You

