



# Developing Selective, Targeted Multi-Cytokine Inhibitors for the Treatment of Immuno-Dermatology and Immuno-Oncology

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# Anti-Cytokine Therapy Has Been Successful in Treating a Variety of Dermatological Diseases

**DUPIXENT<sup>®</sup>**  
(dupilumab)

**IL-4 and IL-13 inhibitor**  
(for atopic dermatitis)

 **Cosentyx<sup>®</sup>**  
(secukinumab)

**IL-17A inhibitor**  
(for plaque psoriasis)

**IL-2, IL-9, and IL-15 Are Implicated in Other Skin Diseases**

**Cutaneous T-cell lymphoma (CTCL)**



**Alopecia Areata (AA)**

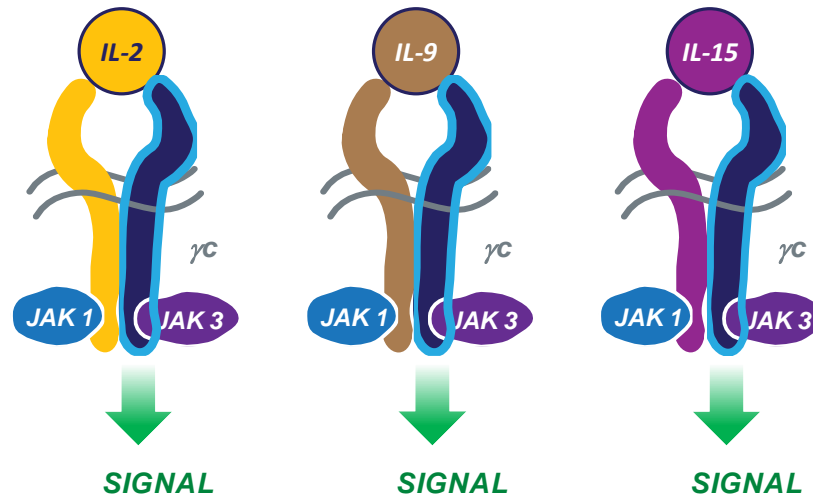


**Vitiligo**

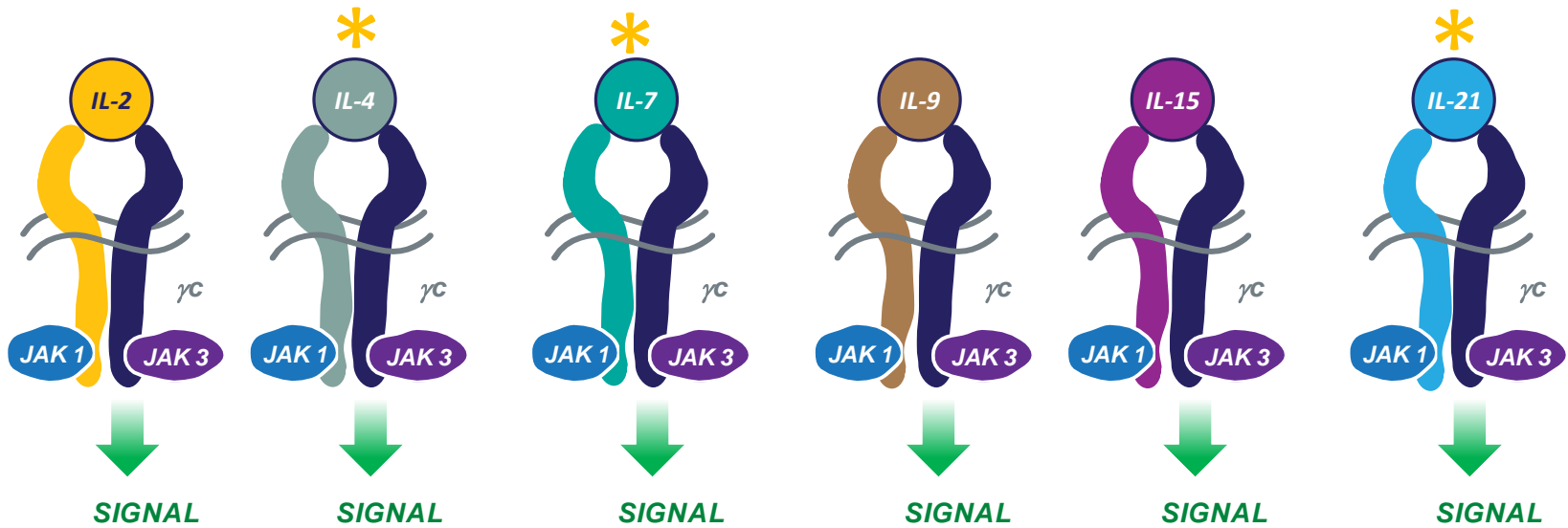


# Designing BNZ-1: an IL-2, IL-9, and IL-15 Inhibitor

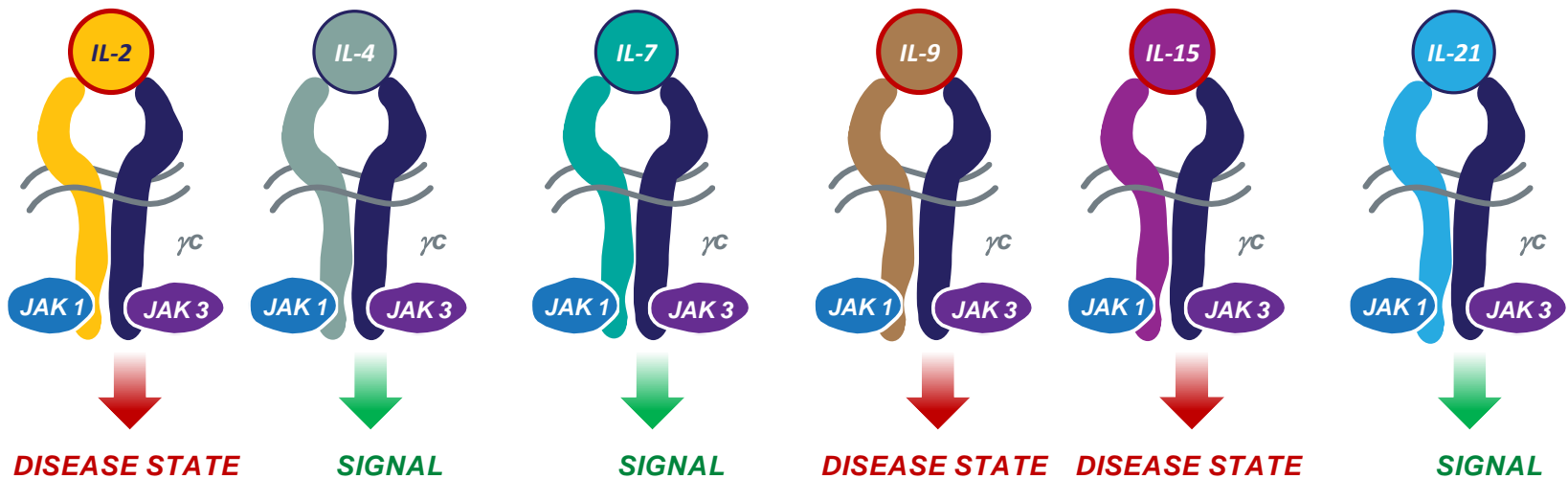
IL-2, IL-9, and IL-15 share a common receptor, called common gamma-c ( $\gamma_c$ )



But the same  $\gamma_c$  receptor is also shared with 3 other cytokines: IL-4, IL-7, IL-21



In CTCL, AA, and Vitiligo IL-2, IL-9, and IL-15 are overexpressed and drive the pathology

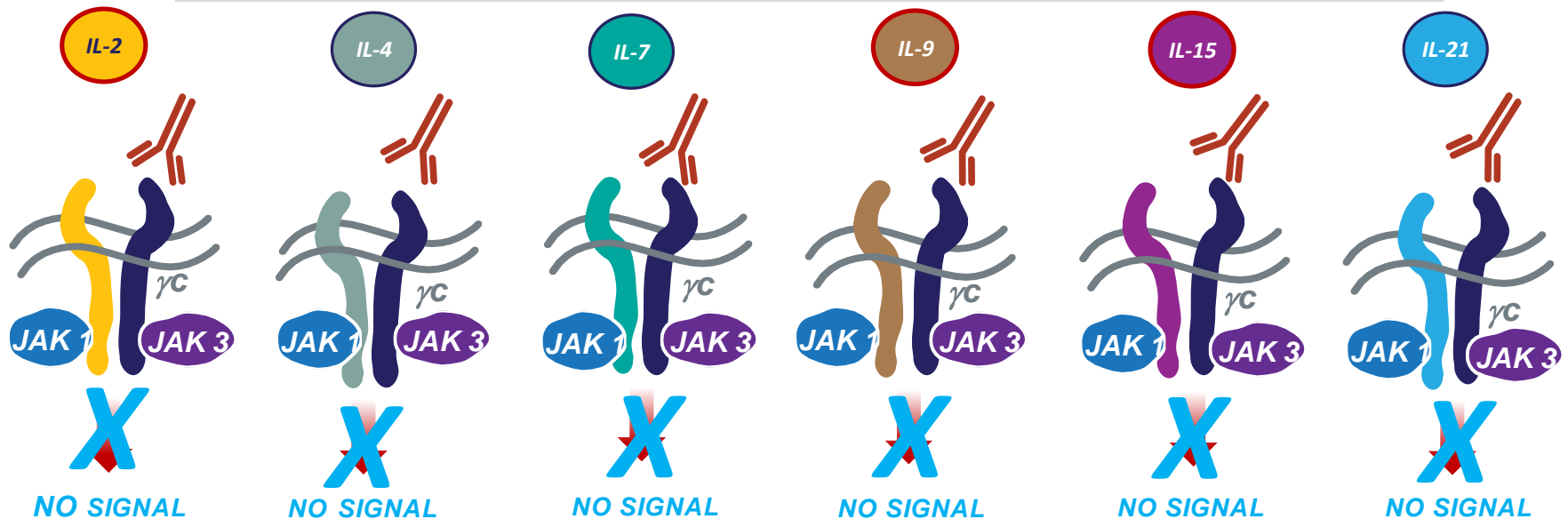


What is the best strategy to selectively target and inhibit IL-2, IL-9, and IL-15?

conventional strategies:

1- generating a mAB against the common receptor

Fact: individuals with a natural non-functional mutation in the common receptor have severe-combined immunodeficiency (no B, T, or NK cells)



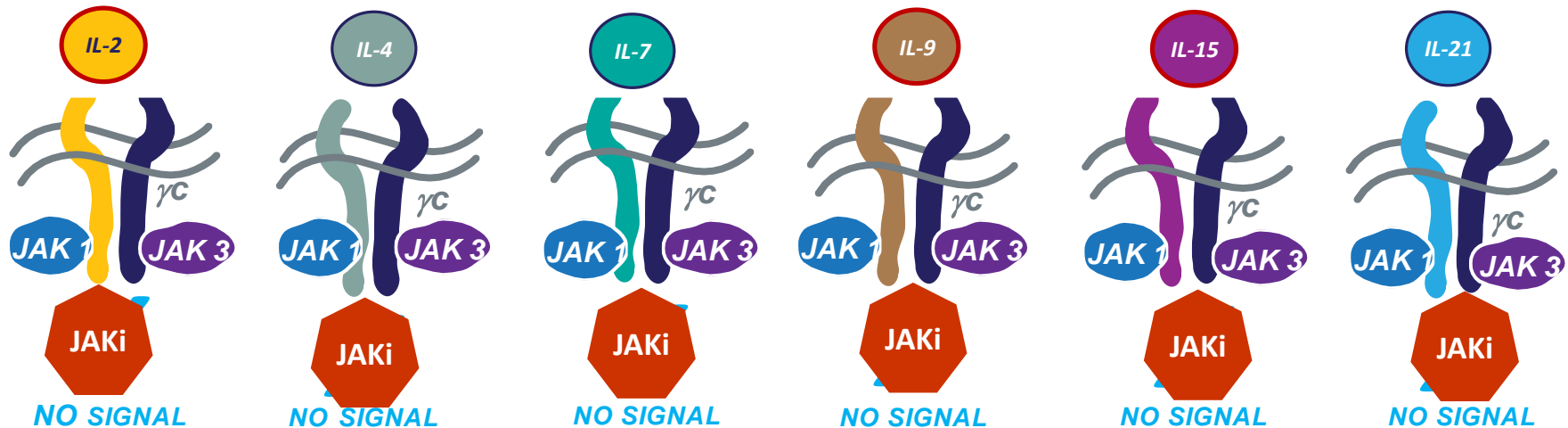
Inhibition of the γC receptor by a mAB or JAKi is not a preferred approach due to potential serious safety concerns

conventional strategies:

- 1- generating a mAB against the common receptor
- 2- using JAK inhibitors to block the downstream signaling

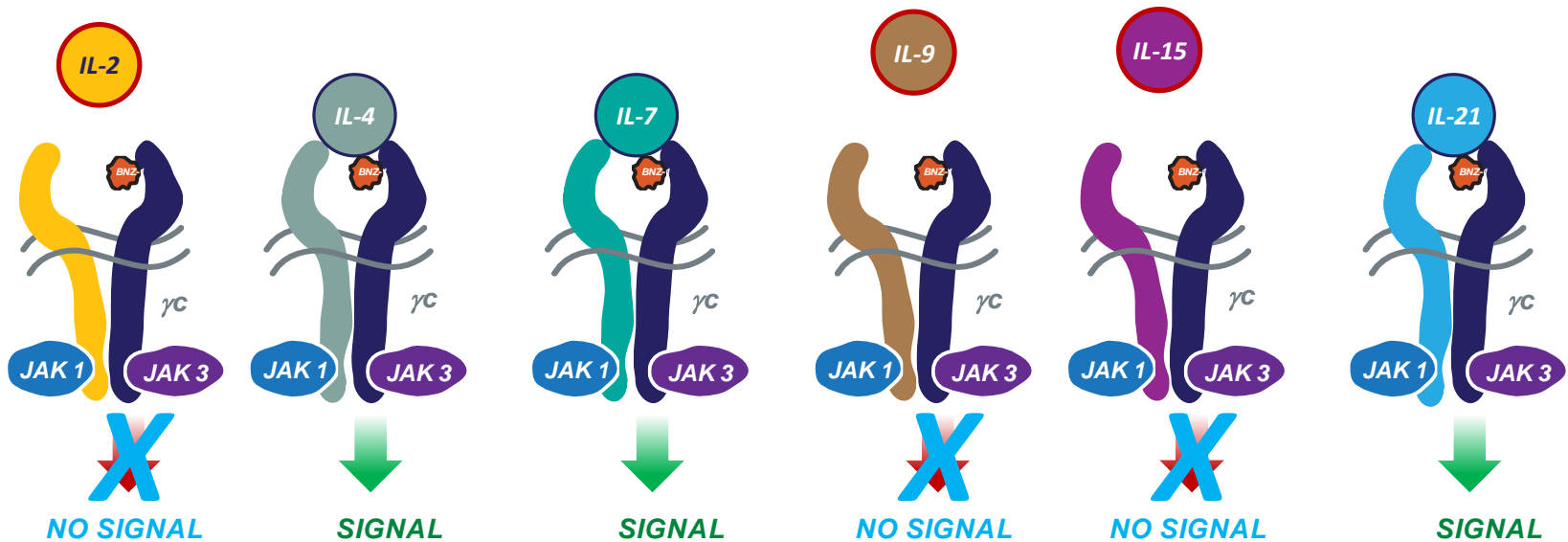
Both approaches will result in inhibition of all the six cytokines → potential to develop severe immunodeficiency

Fact: individuals with a natural non-functional mutation in the common receptor have severe-combined immunodeficiency (no B, T, or NK cells)



Inhibition of the  $\gamma_C$  receptor by a mAB or JAKi is not a preferred approach due to potential serious safety concerns

**BNZ-1 is a PEGylated peptide that selectively inhibits IL-2, IL-9, and IL-15 and not the other cytokines in this family**



**BNZ-1 provides a highly targeted inhibition of cytokines that are disease drivers**



# BNZ-1 Has Been Tested in Two Clinical Trials: Phase I Study in Healthy Volunteers and Phase I/II Study in CTCL Patients

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## Phase I trial in healthy subjects:

**43 healthy subjects treated with BNZ-1 across studies**

- ✓ No dose-limiting toxicities
- ✓ No serious or severe effects
- ✓ No infusion reactions
- ✓ No clinical lab abnormalities

## Phase I/II trial in refractory CTCL patients:

**A dose ranging study was completed across 4 doses**

(0.5, 1, 2, and 4 mg/kg)

- ✓ No dose-limiting toxicities
- ✓ Well tolerated
- ✓ No infusion reactions
- ✓ Preliminary efficacy was observed in some cohorts allowing for dose expansion

# Preliminary Efficacy Data in Refractory CTCL Patients Observed After BNZ-1 Treatment

Baseline



Week 16



A dose expansion study at 2 mg/kg is ongoing to substantiate the safety and efficacy of BNZ-1 in CTCL patients

- Top line data expected in Q2 2020

# BNZ-1: Pipeline In a Product For An Immuno-Dermatology Franchise

- **BNZ-1 is a selective inhibitor of IL-2, IL-9, and IL-15**
- **BNZ-1 has shown excellent safety profile in healthy subjects and CTCL patients**
- **BNZ-1 has shown preliminary clinical efficacy in highly treated refractory CTCL patients → proof of concept**
- **BNZ-1 has clinical utility in treatment of a number of immuno-dermatological disorders with high unmet medical need**
  - **Cutaneous T-Cell Lymphoma (CTCL)**
  - **Alopecia Areata (AA)**
  - **Vitiligo**
- **BNZ-1 addresses multi-billion dollar markets with no or limited standard of care**