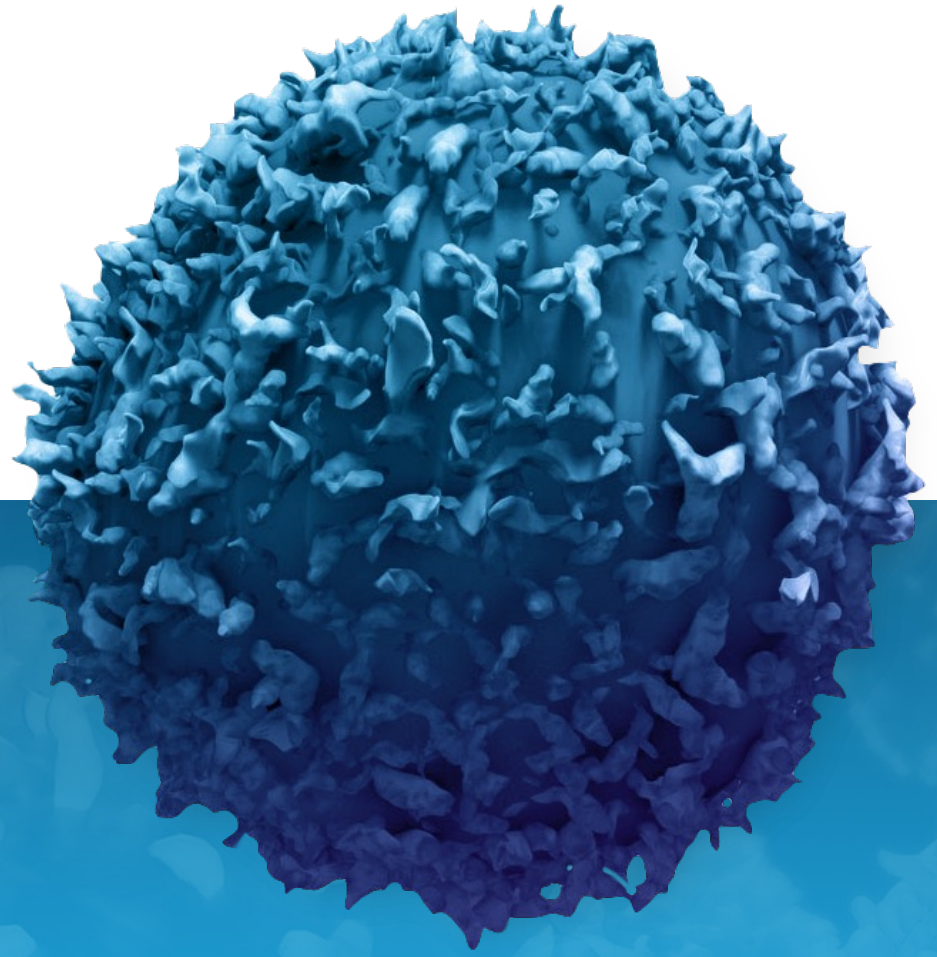
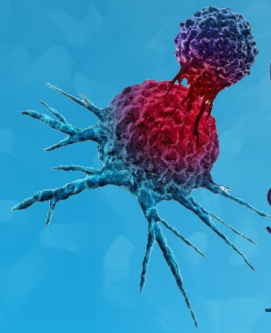


equillium®

Targeting Biological Synergy at the Receptor Level:

Multi-specific Cytokine Inhibitors



Cytokine Based Drug Development Summit

July 26th – 29th 2022, Boston, MA

Forward-Looking Statements

This presentation contains forward-looking statements about Equillium, Inc. (the "Company"). In some cases, you can identify forward-looking statements by the words "will," "expect," "intend," "plan," "objective," "believe," "estimate," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements are based on Company management's current beliefs and expectations. These statements include but are not limited to statements regarding the Company's business strategy, the Company's plans to develop and commercialize its product candidates, the safety and efficacy of the Company's product candidates, the Company's plans and expected timing with respect to regulatory filings and approvals, size and growth potential of the markets for the Company's product candidates and cash runway. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause the Company's actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The Company may not actually achieve the plans, intentions or expectations disclosed in its forward-looking statements, and you should not place undue reliance on the Company's forward-looking statements.

Actual results or events could differ materially from the plans, intentions and expectations disclosed or implied in the forward-looking statements the Company makes due to the risks and uncertainties inherent in the Company's business, including without limitation, risk described in the Company's filings with the Securities and Exchange Commission ("SEC"). You are cautioned not to place undue reliance on these forward-looking statements, which represent the Company's views as of the date of this presentation. The Company's anticipates that subsequent events and developments will cause the its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company has no current intention of doing so except to the extent required by applicable law. These and other risks and uncertainties are described more fully under the caption "Risk Factors" and elsewhere in the Company's filings and reports, which may be accessed for free by visiting EDGAR on the SEC web site at http://www.sec.gov and on the Company's website under the heading "Investors." All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the "safe harbor" provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.

Cytokine Signaling – A Complex and Combinatorial Issue

This same complexity shown in how cytokines signal to regulate immune homeostasis presents unique drug development challenges when treating disease

Three important characteristics of most cytokines are:

1. ***Pleiotropy*** - the ability of one cytokine to exhibit diverse biological activities
2. ***Redundancy*** - the ability of multiple cytokines to exert overlapping biological activities
3. ***Synergy*** - the ability of multiple cytokines to cooperate to change biological activities

e.g., anti-IL-4Ra

Use of shared receptors

Common γ-chain (γc), GP130, beta chain (βchain)

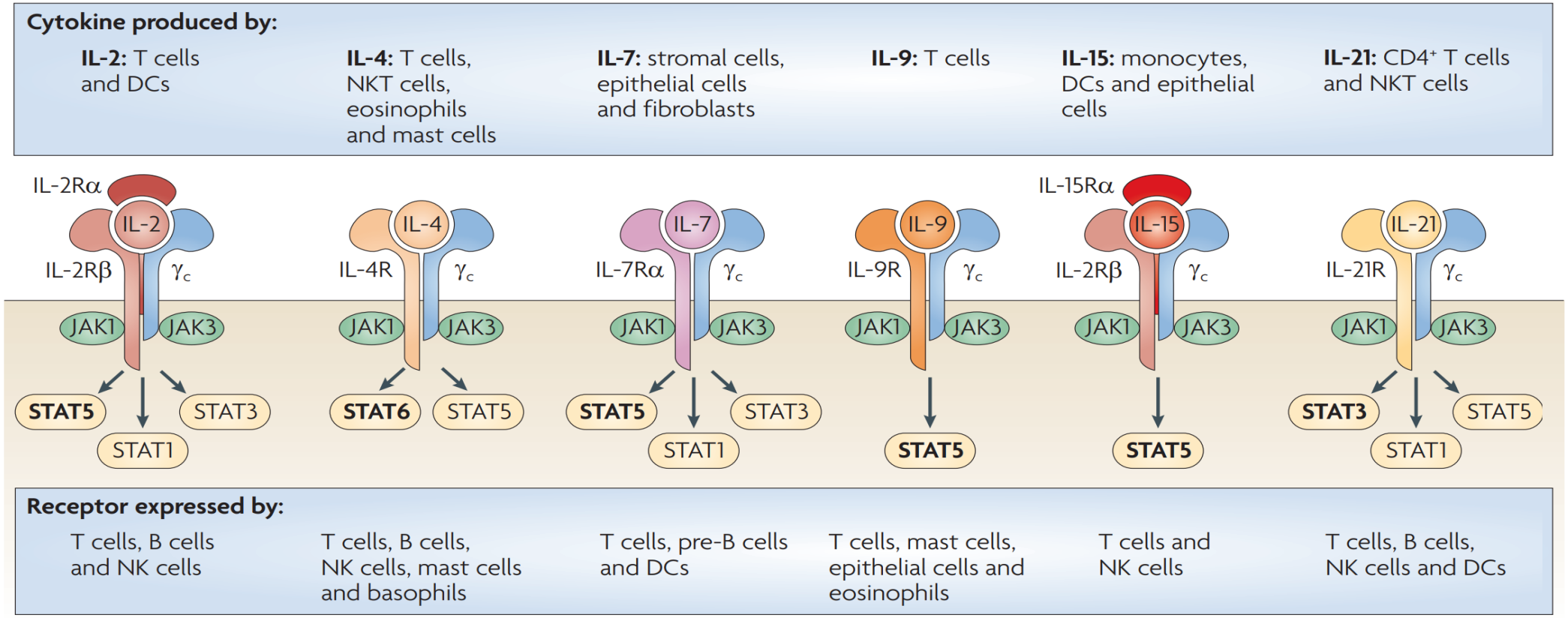
Balance of intra- and inter- cellular signals

JAK/STAT, RAF/Erk, PIK3/mTor

e.g., JAK inhibitors

Targeting the γc Receptor, a Key Cytokine Signaling Hub

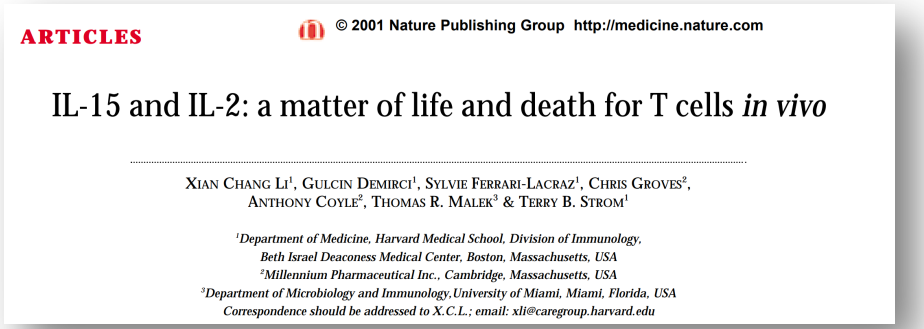
Cytokines signaling through the common gamma (γc) chain exhibit ***redundancy*** as well as ***synergy*** that has been shown to be ***important to pro-inflammatory disease states***



Biological Redundancy and Synergy at the yc Receptor

IL-2 / IL-15

- Overlap in activity of IL-2 / IL-15 on CD8 and NK T cells
- Synergy in between IL-2 and IL-15 in determining cell fate
- Synergy in between cell types expressing IL-2 and IL-15 during inflammation



ARTICLES

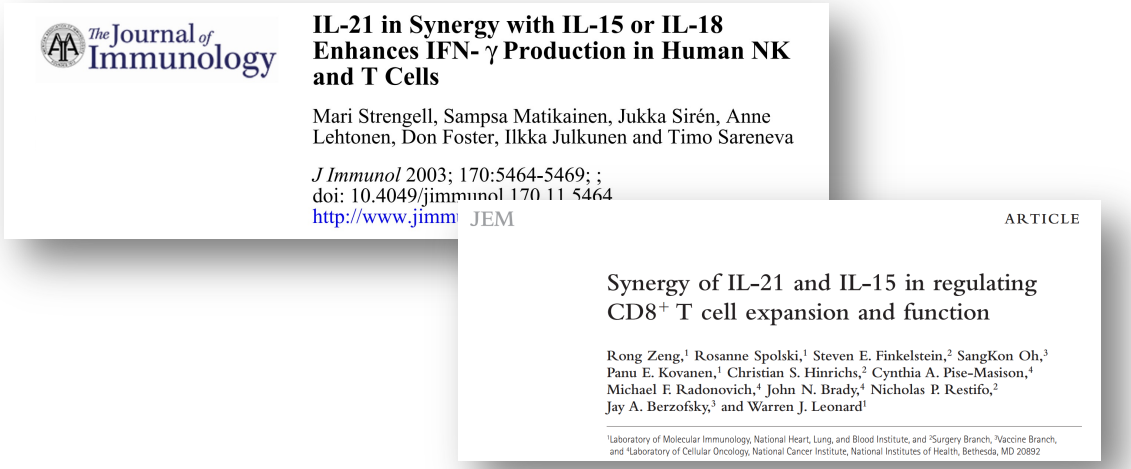
IL-15 and IL-2: a matter of life and death for T cells *in vivo*

XIAN CHANG LI[1], GULCIN DEMIRCI[1], SYLVIE FERRARI-LACRAZ[1], CHRIS GROVES[2], ANTHONY COYLE[2], THOMAS R. MALEK[3] & TERRY B. STROM[1]

[1]*Department of Medicine, Harvard Medical School, Division of Immunology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA*
[2]*Millennium Pharmaceutical Inc., Cambridge, Massachusetts, USA*
[3]*Department of Microbiology and Immunology.University of Miami, Miami, Florida, USA*
Correspondence should be addressed to X.C.L.; email: xli@caregroup.harvard.edu

IL-15 / IL-21

- Synergy in between IL-15 and IL-21 to potently promote the proliferation of both naïve and memory CD8 T cells
- IL-21 enhanced IL-15-induced IFN-γ gene expression



The Journal of Immunology

IL-21 in Synergy with IL-15 or IL-18 Enhances IFN- γ Production in Human NK and T Cells

Mari Strengell, Sampsa Matikainen, Jukka Sirén, Anne Lehtonen, Don Foster, Ilkka Julkunen and Timo Sareneva

J Immunol 2003; 170:5464-5469; ;
doi: 10.4049/jimmunol.170.11.5464
http://www.jimm

JEM ARTICLE

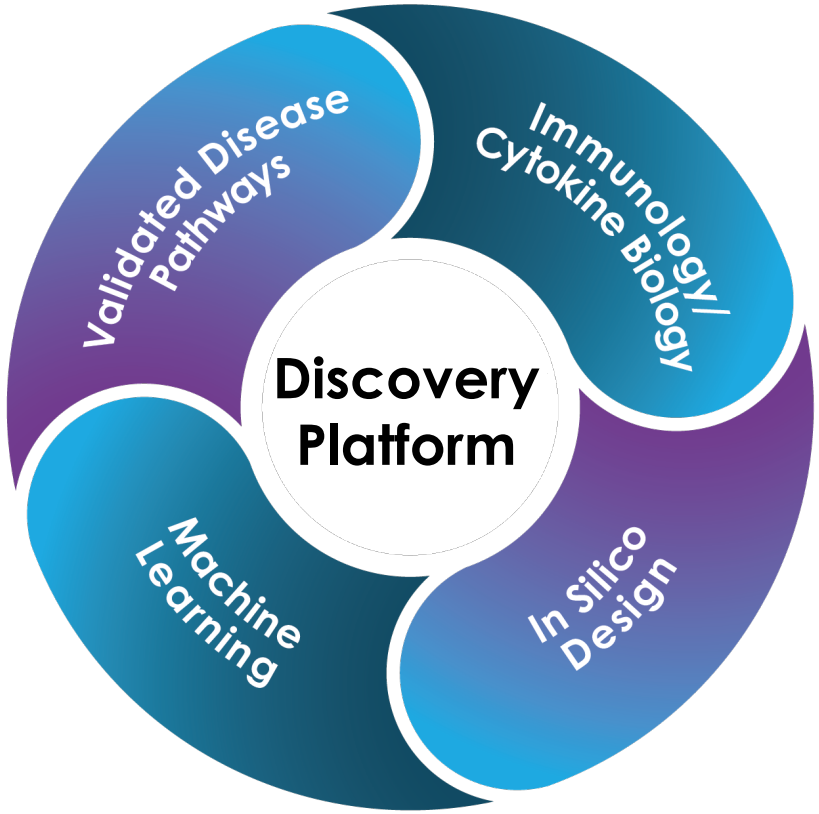
Synergy of IL-21 and IL-15 in regulating CD8$^+$ T cell expansion and function

Rong Zeng,[1] Rosanne Spolski,[1] Steven E. Finkelstein,[2] SangKon Oh,[3] Panu E. Kovanen,[1] Christian S. Hinrichs,[2] Cynthia A. Pise-Masison,[4] Michael F. Radonovich,[4] John N. Brady,[4] Nicholas P. Restifo,[2] Jay A. Berzofsky,[3] and Warren J. Leonard[1]

[1]Laboratory of Molecular Immunology, National Heart, Lung, and Blood Institute, and [2]Surgery Branch, [3]Vaccine Branch, and [4]Laboratory of Cellular Oncology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892

Discovery Platform – Multi-cytokine Inhibitors

Novel product platform addresses the limitations of single-target biologics and broadly immunosuppressive therapies (e.g. JAKi) through peptide-based multi-cytokine inhibition

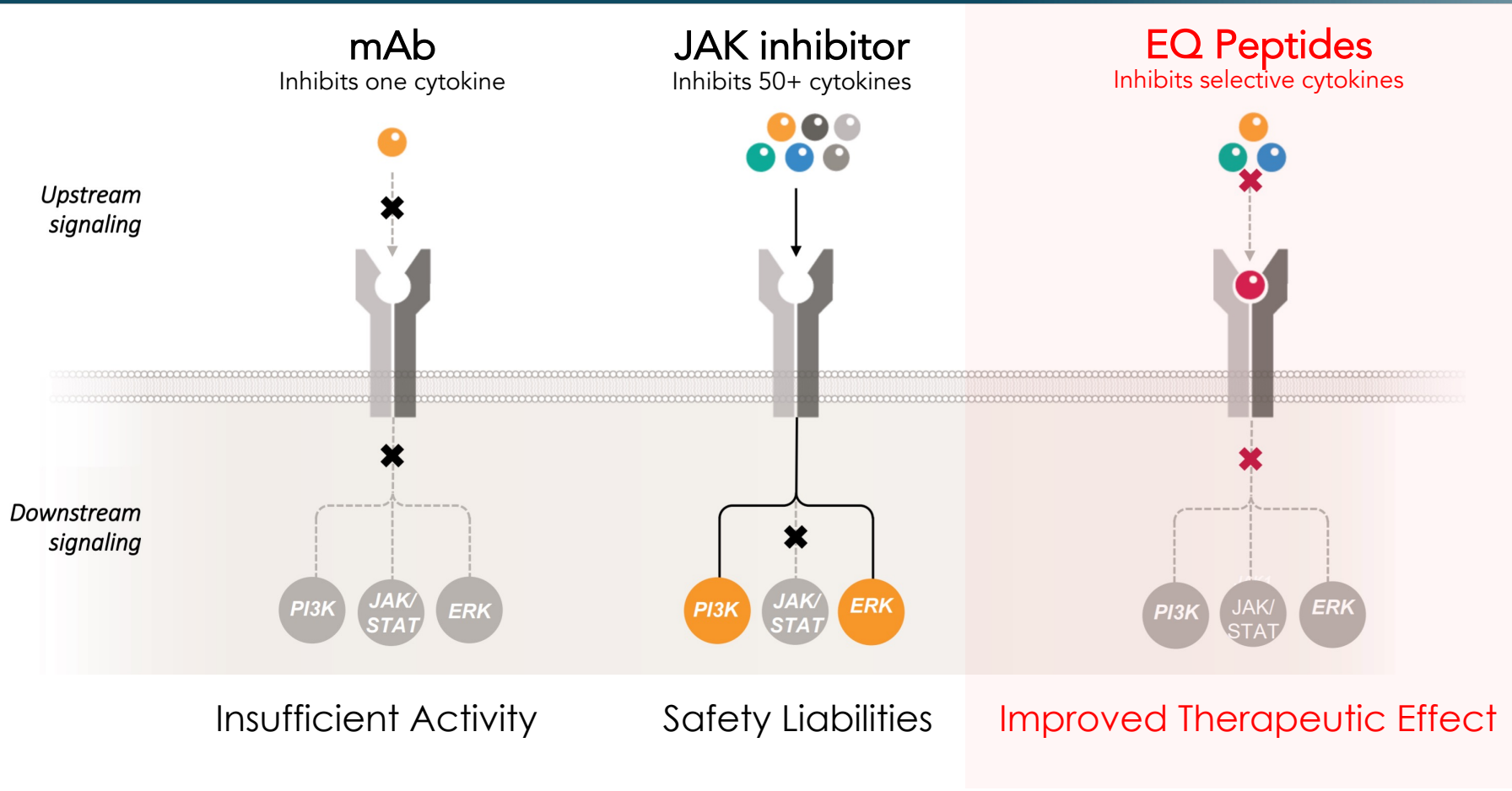


- Targeting validated biological and disease pathways
- Leveraging in-house expertise in immunology and cytokine biology
- Using *in silico* computational modeling to design candidate peptides
- Analyzing structure-activity relationships and combining with machine learning to optimize binding

"The new class of peptides inhibiting different combinations of cytokines tailored to different diseases exploiting the redundancy or synergy in cytokine biology"

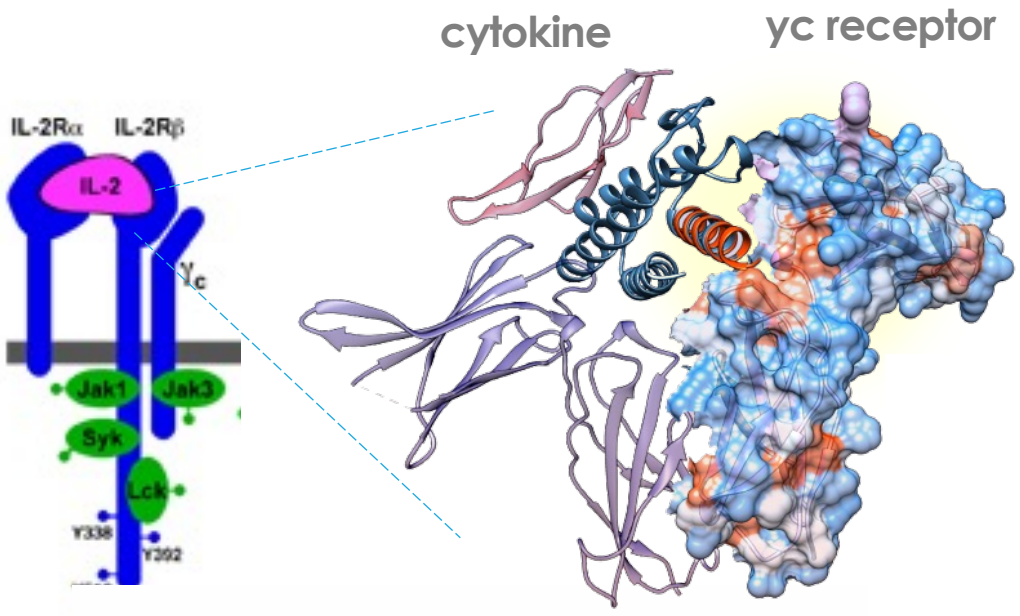
Optimized Modality Compared to mAbs and JAK Inhibitors

Multi-cytokine inhibition at the receptor-level without the broad immuno-suppression and off target safety liabilities of JAK inhibitors



EQ101 Validates EQ's Unique Structure-Based Discovery Platform

Cytokine-receptor binding interface




```
IL-15   ----------ECEEIKEFLQSFVHIVQMFI--NTS
IL-2    ----------TIVEFLNRWITFCQSII-STLT
IL-21   ----------PLEFLERFKSLLQKMIHQHLS
IL-4    ----------NQSTLENFLERLKTIMREKYSKCSS
IL-7    LEENKSLKEQKKL-NDLCFLKRLLQEIKTCW-NKIL
IL-9    ----------NALTFLESLLELFQKEKMRGMR
                  **:      :
```

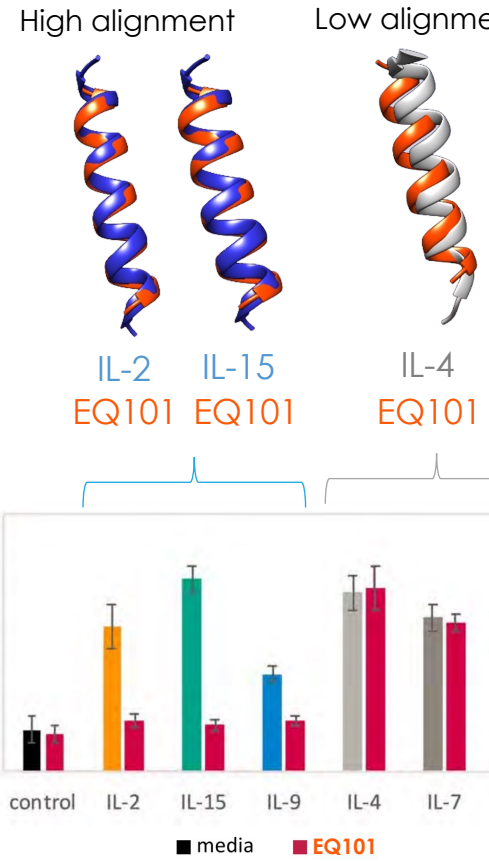
The γc box

Binding optimization via proprietary methodology:

- *in silico* computational modeling
- Structure-activity relationships

EQ101 Structured-Domain Peptide

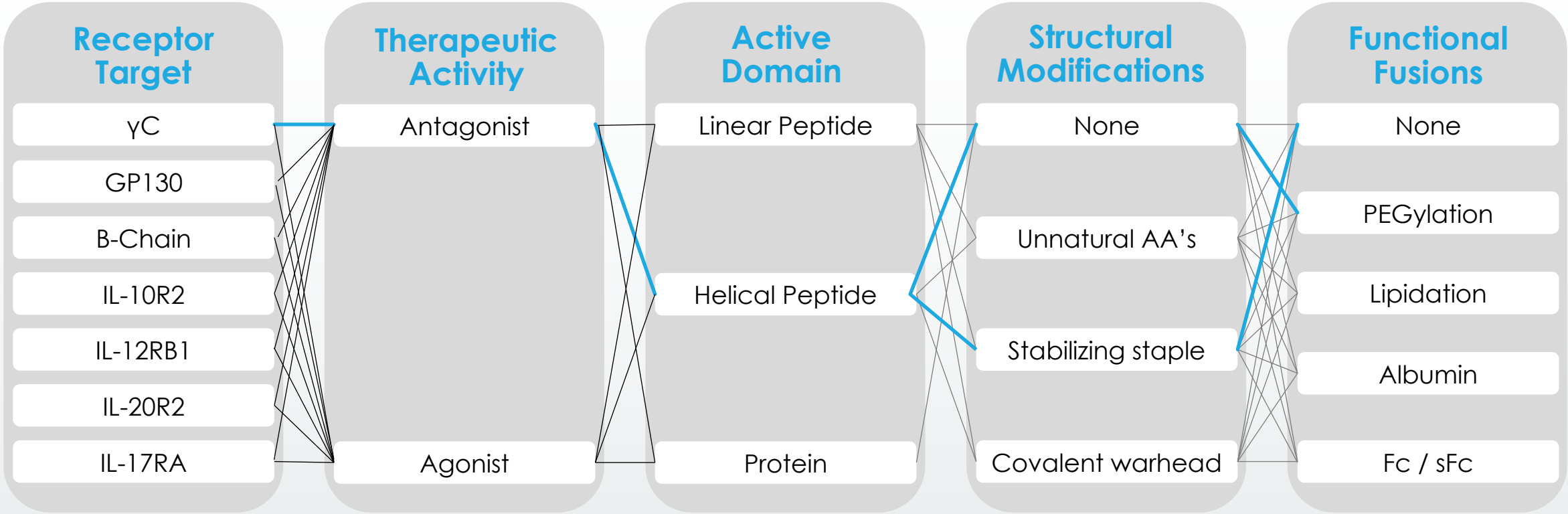
High alignment with IL-2 and IL-15 and low alignment with IL-4 correlates with EQ-101's ability to block IL-2 and IL-15 activity, but not IL-4 activity



Nata *et al.*, 2018

Creating Value through Novel Product Discovery Platform

Flexible, structure-based discovery technology enables development of a range of therapeutic agents (antagonists/agonists) with tunable drug-like properties



Differentiated Lead Assets & Broad Platform Potential

EQ101

PEGylated peptide inhibits:

IL-2 + IL-9 + IL-15

Cutaneous T Cell Lymphoma
Alopecia areata
Vitiligo
Rheumatoid arthritis
Myositis
Interstitial lung disease

Administered by intravenous injection with subcutaneous delivery in development

EQ102

PEGylated peptide inhibits:

IL-15 + IL-21

Celiac disease
Inflammatory Bowel Disease
SLE
Hepatic disease
Type 1 Diabetes

Administered by subcutaneous injection

Advanced Pre-clinical

Stabilized peptide Inhibits:

IL-15 + IL-21

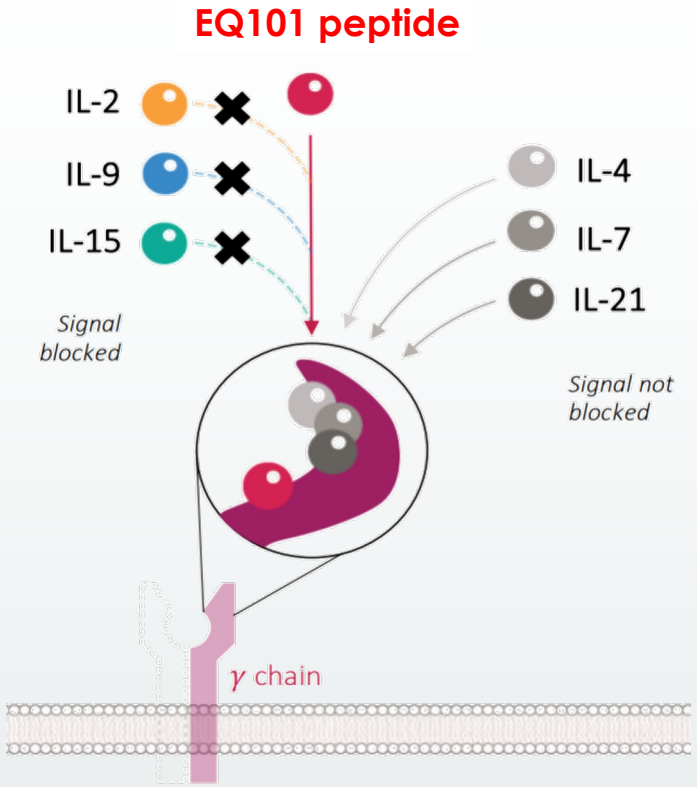
GI-inflammatory disorders

Orally-delivered, locally-acting peptide

EQ101 A First-in-class Tri-Specific Cytokine Inhibitor

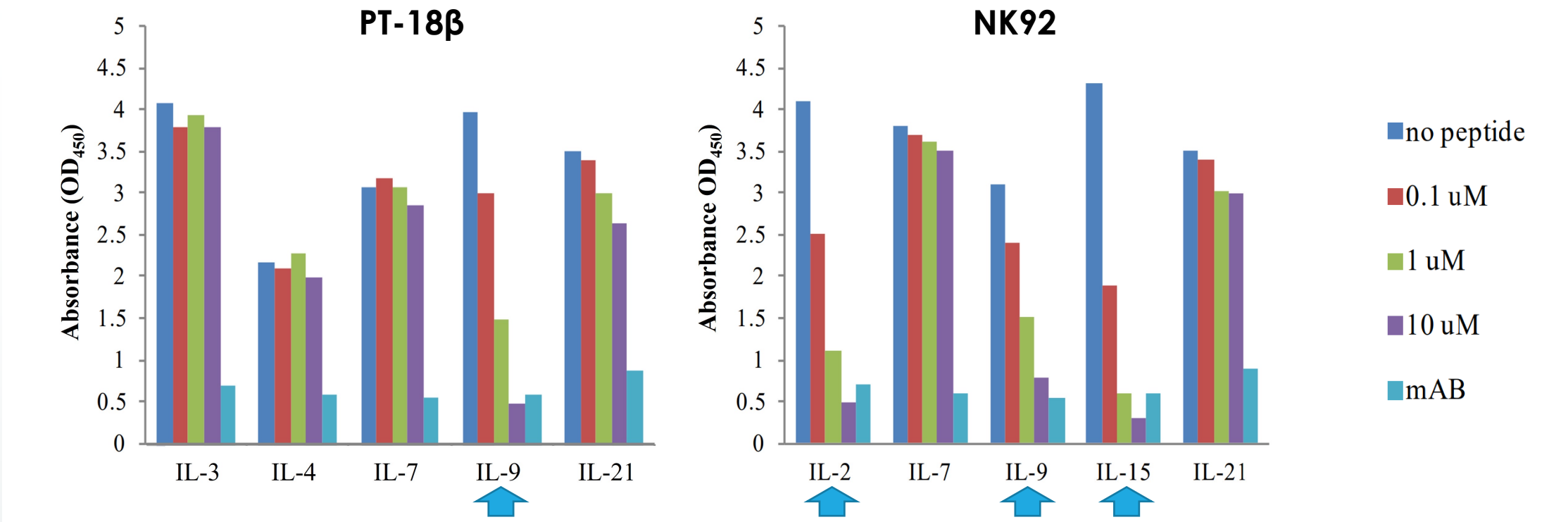
Inhibition of IL-2, IL-9, and IL-15 biology by EQ101 translates from preclinical models into humans

- IL-2 and IL-15 are important to CD8 and NK cell biology, while IL-9 contributes to inflammation
- Pegylated peptide based on D-helix selectively inhibits IL-2/9/15 without suppressing other γ chain or non-γ chain cytokines
- EQ101 inhibits T cell biology in multiple preclinical models
  - As good as anti-IL-2/IL-15 mAb combo in inhibiting T cell proliferation[1]
  - Inhibition of activity in multiple lymphoproliferative or leukemic T-cell lines[2,3]
  - EQ101 is more effective than ruxolitinib or anti-IL-2/anti-IL-15 combinations in mouse model of alopecia areata



1) Nata et al., 2015; 2) Massoud et al., 2015; 3) Wang et al., 2018;

EQ101 Selectively Inhibits γc Cytokines IL-2/IL-9/IL-15

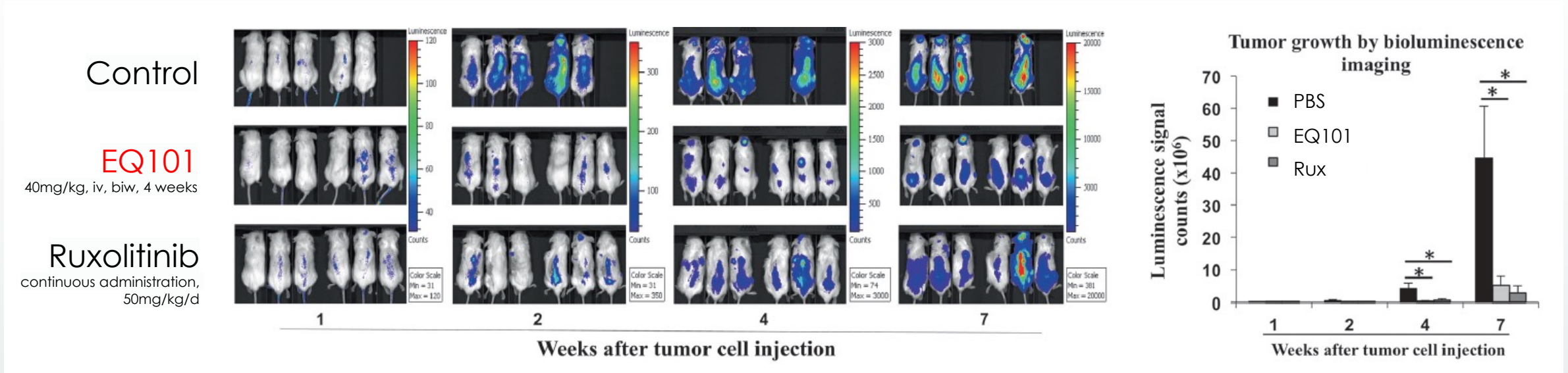


PT-18β and NK92 cells were brought to a resting state by washing and culturing in complete RPMI media in the absence of the cytokine for 6 hrs. Cells were then plated at $1x10^5$ per well in a 96 well plate. Each assay was tested in triplicates. The cells were cultured with cytokine, antibody against cytokine (5 µg/ml), and serial dilution of EQ101. WST-1 reagent was added to each well 24 hrs after and the plate was read 24 hrs after that at 450 nm

1)In-house data and Nata et al., 2015

EQ101 Inhibits T cell Leukemia Growth in a Xenograft Model

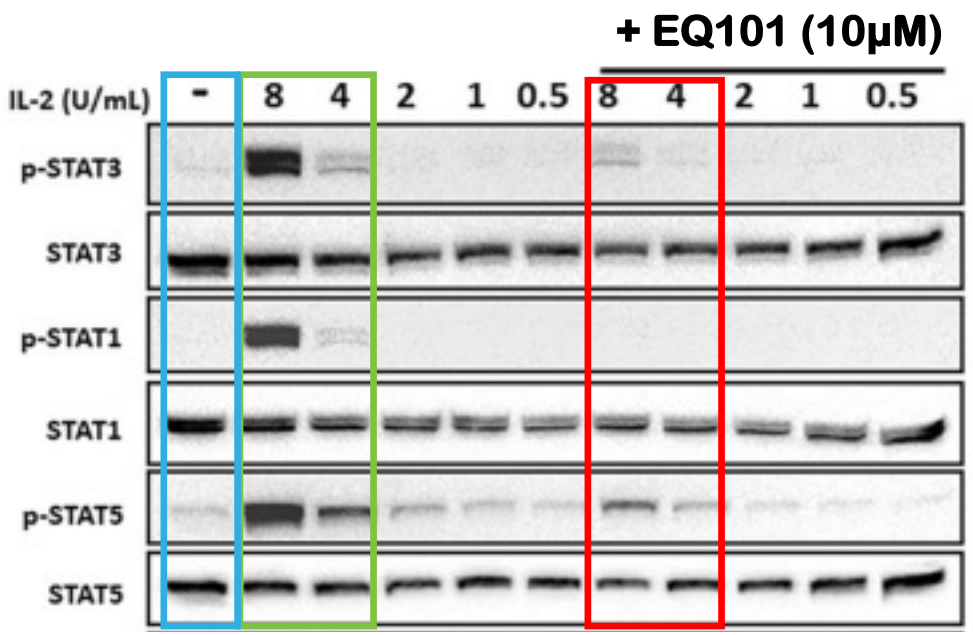
- IL-2, IL-9, and IL-15 are overexpressed in adult T cell leukemia (ATL) and cutaneous T cell lymphoma (CTCL) where they drive cancer cell proliferation and increased inflammation in the skin[1,2,3,4,5]
- Blocking IL-2 or IL-15 alone was ineffective in treating LGLL[6] and ATL[7]
- EQ101 inhibits IL-2/9/15 performing similarly to JAK inhibition in an IL-15 driven ATL model[8]



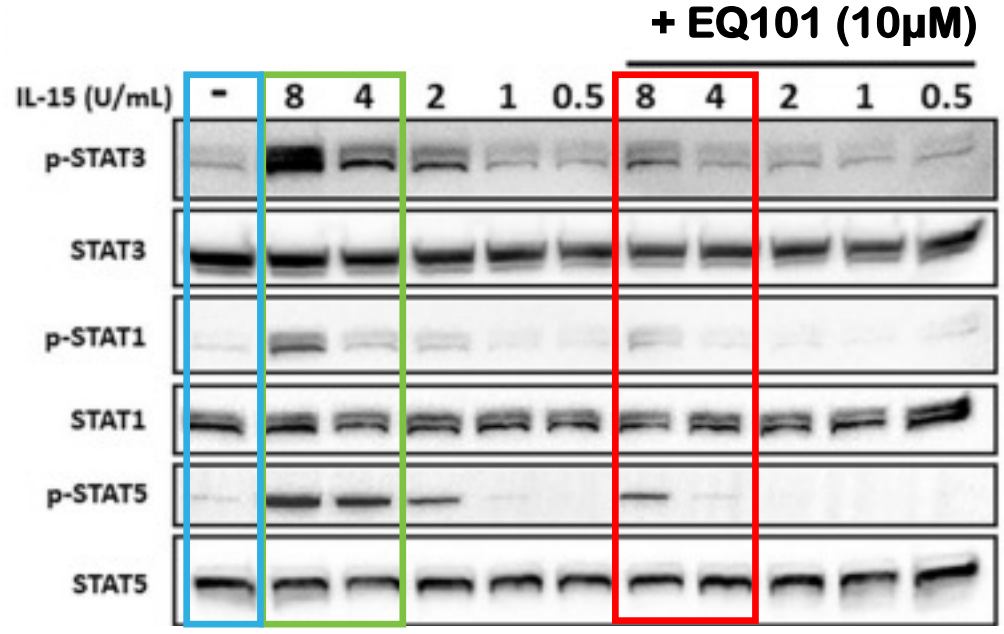
1) Dobbeling et al.,1998 2) Mishra et al., 2016 3) Qin et al., 2001 4) Garcia et al., 2016 5) Waldmann et al., 1993 6) Waldmann et al., 2013 7) Berkowitz et al., 2014 8) Wang et al., 2018

EQ101 Inhibits IL-2 and IL-15 Induced STAT Activity

IL-2



IL-15



Wang et al., 2018

First-in-human Studies of EQ101

Study ID	Phase/Study Type	Study Title	Dosing Regimens Studied
BNZ-CT-101	Phase 1a First in Human SAD	First in Human Study in Healthy Volunteers to Investigate the Safety, Tolerability, and Pharmacokinetics of Single Ascending Doses of BNZ132-1-40	Single IV doses of: • 0.2 mg/kg (N=3) • 0.4 mg/kg (N=3) • 0.8 mg/kg (N=3) • 1.6 mg/kg (N=3) • 3.2 mg/kg (N=3) • 6.4 mg/kg (N=3)
BNZ1-CT-102	Phase 1b MAD	A Multiple-Dose Study of Intravenous BNZ132-1-40 in Healthy Adult Subjects	Three (for QOW doses) or four (for QW doses) IV doses of: • 0.5 mg/kg QW (N on Treatment=5, 1 Placebo) • 1.0 mg/kg QW (N on Treatment=5, 1 Placebo) • 2.0 mg/kg QOW (N on Treatment=5, 1 Placebo) • 1.5 mg/kg QW (N on Treatment=5, 2 Placebo) • 3.0 mg/kg QOW (N on Treatment=5, 2 Placebo)

- No dose-limiting toxicities, infusion reactions, or serious or severe treatment-emergent adverse events
- Peak and total BNZ-1 exposure was generally dose proportional, with a terminal elimination half-life of approximately a week
- Dose-dependent decreases in key target cells (NK and CD8 etc) with observed for beyond two weeks with higher doses

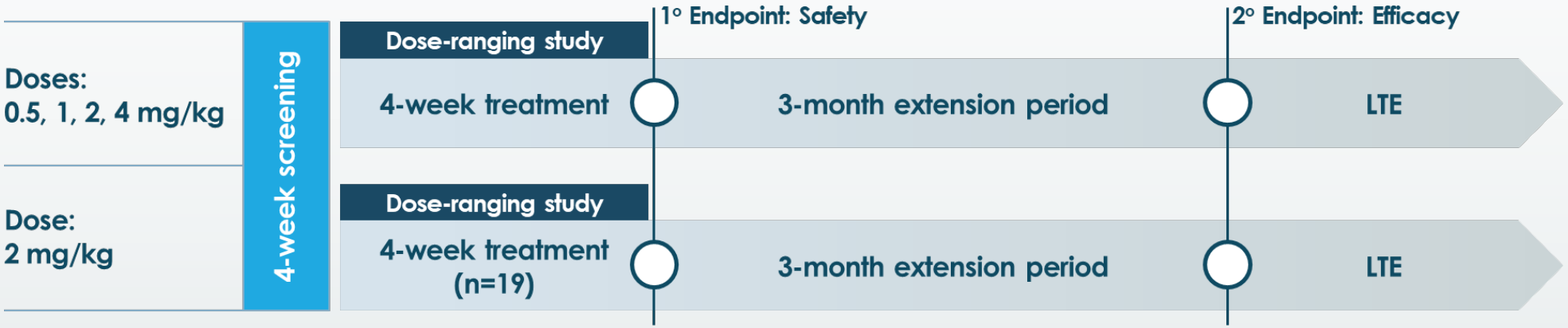
Frohna *et al.*, 2020

Phase 1/2 Proof of Concept Study of EQ101 in CTCL Patients

Clinically validated with favorable safety profile, Phase 2/3 ready to address multiple indications with significant unmet medical need

Phase 1/2 MAD study in CTCL

- Heavily pre-treated population (median of 5 prior systemic treatments)
- Dose-dependent PK/PD relationship in key cellular markers
- Safe and well-tolerated with no drug related SAEs, no DLTs and no clinically significant laboratory abnormalities
- Dose-dependent reductions of IL-2 & IL-15 dependent cells and improvements in mSWAT



Querfeld et al., ASH 2020

EQ101 Clinically Validated in Severe Dermatological Disease

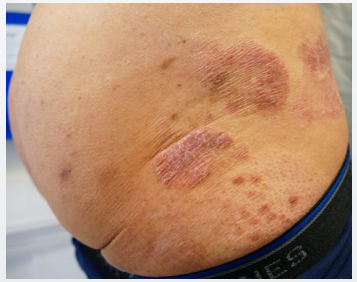
EQ101 reduces IL-2 & IL-15 dependent cells and inflammation with improvements in skin lesions and ORR comparing favorably with benchmark drugs

MAVORIC trial evaluating mogamulizumab and vorinostat provides the most recent and reliable estimates for benchmarking EQ101[1]

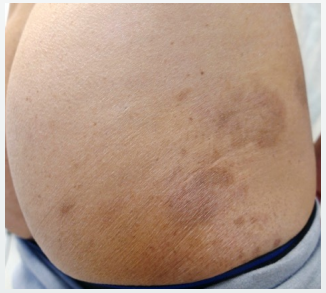
	CTCL disease stage IB/II		
	Mogamulizumab (n=68)	Vorinostat (n=72)	**EQ101 (n=19)**
Response Rate (mSWAT, CR + PR)	27.9%	19.4%	**42.1%[2]**

EQ101, 2mg/kg

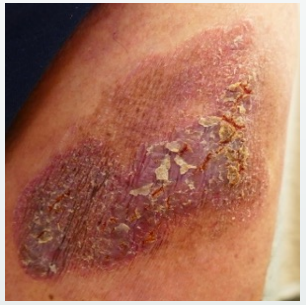
Baseline



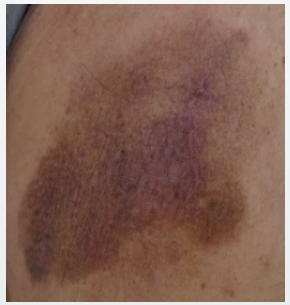
Week 16



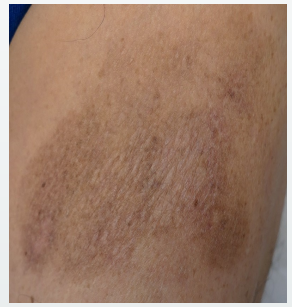
Baseline



Week 16



Week 31



1) Kim et al. 2018. 2) Two additional patients achieved PR but are not included since they did not reach 4 weeks of response due to termination of the study. Including those patients response rate =52.6% 3) Patients shown were entered into the long-term extension portion of BNZ1-CT-201 and continued to be dosed for over 70 weeks. mSWAT = modified severity-weighted assessment tool

EQ101: Cutaneous T Cell Lymphoma

Inhibition of IL-2/9/15 translates from in vitro/ex vivo models into patients with clinical efficacy and favorable safety and tolerability profile

Strong biologic rationale

- IL-2, IL-9, and IL-15 are overexpressed in adult T cell leukemia (ATL) and cutaneous T cell lymphoma (CTCL) where they drive cancer cell proliferation and increased inflammation in the skin
- Inhibition of activity in multiple lymphoproliferative or leukemic T-cell lines

Planned Phase 2/3 Ready

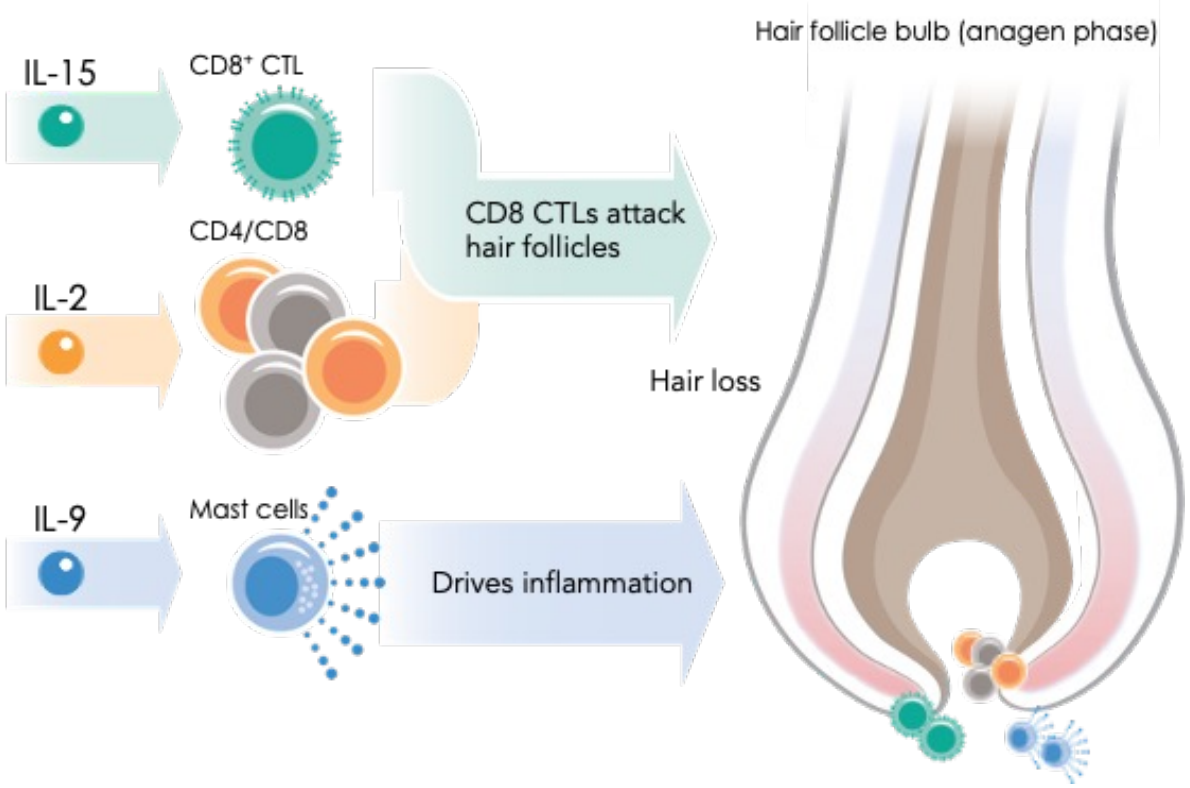
- Demonstrated inhibition of IL-2/IL-15 dependent inflammation with improvements in skin lesions
- IND open for Phase 3 study

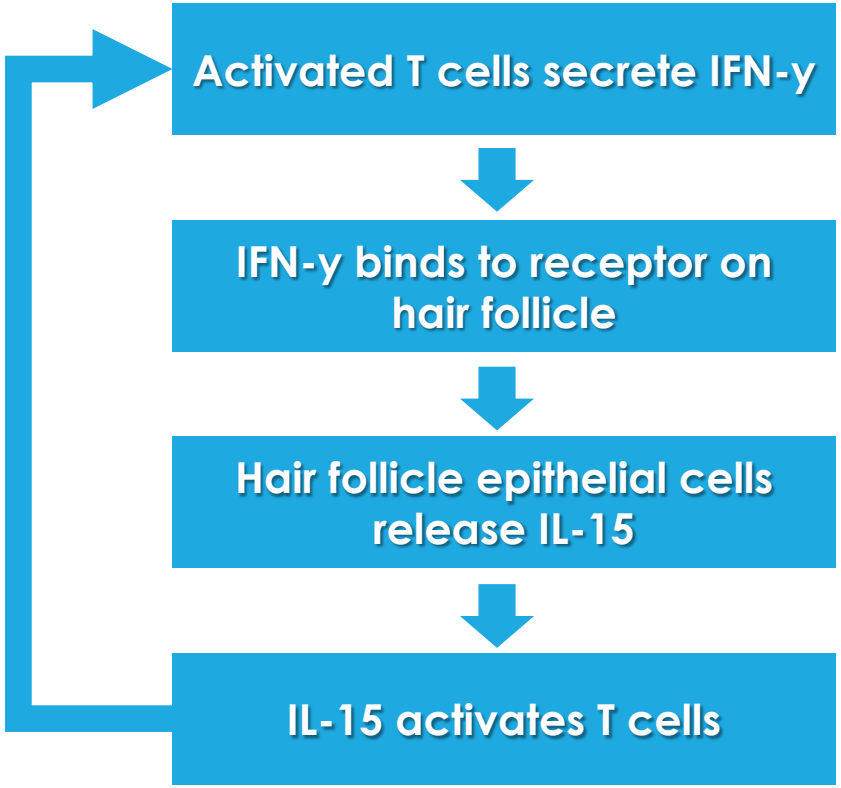
Rare disease with high unmet medical need

- 30,000 addressable patients in U.S. alone
- Need for a safe and effective treatment for skin-stage disease (mycosis fungoides)

Alopecia Areata - Pathophysiology

The targets for EQ101 inhibition (Il-2, IL-9 and IL-15) are key drivers of disease leading to a cycle of increased IFN-y production and loss of hair follicle in alopecia areata patients



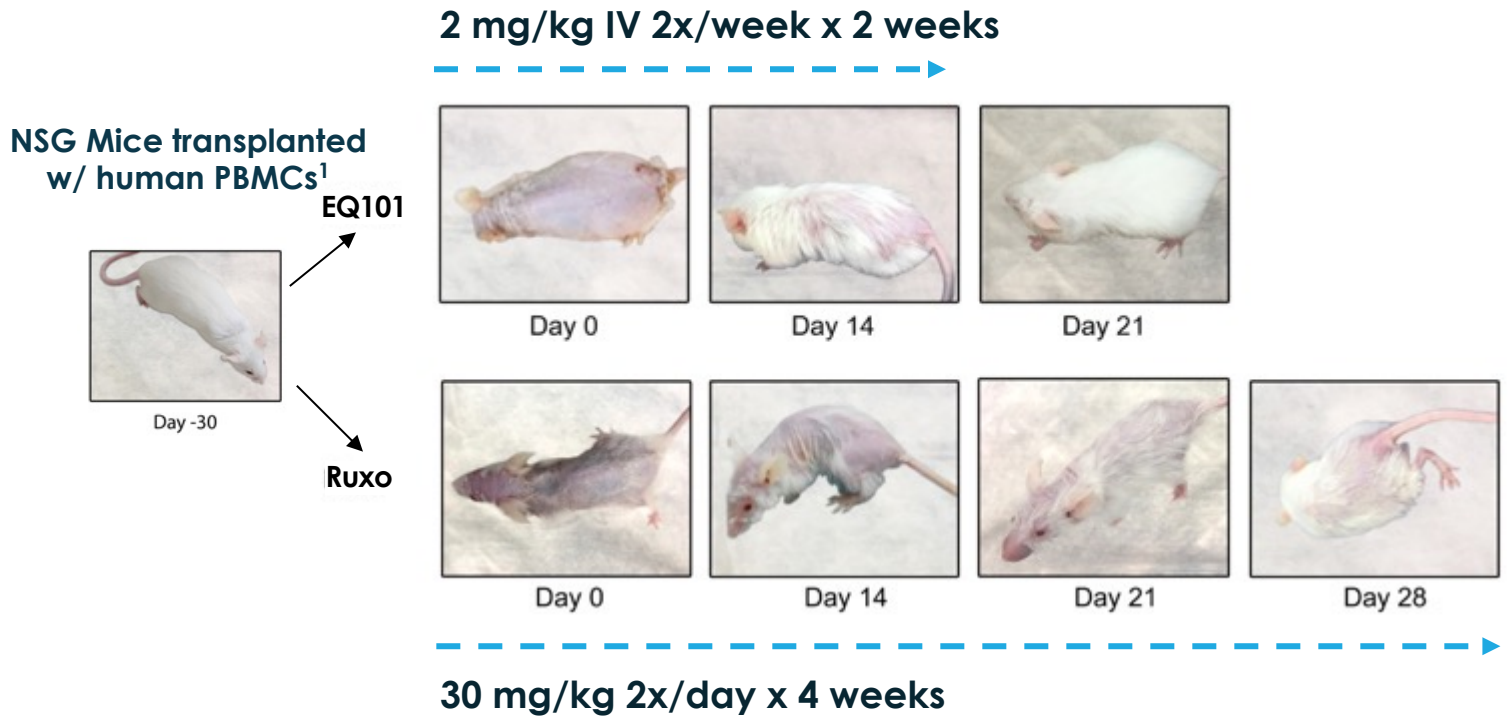


Xing *et al.*, 2014; Bertolini *et al.*, 2014; Suarez-Farinas *et al.*, 2015; Dai *et al.*, 2001

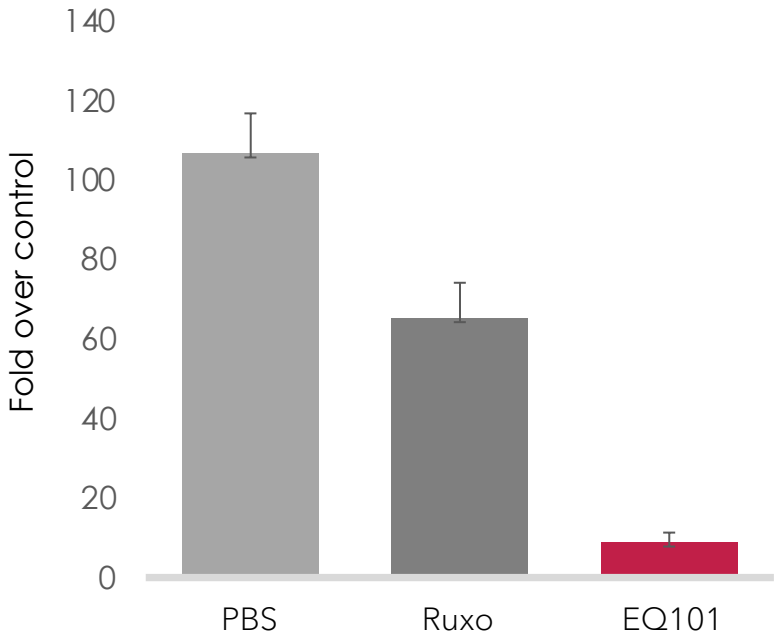
EQ101 Outperforms Ruxolitinib in Reversing Immune-Mediated Hair Loss in a Humanized Mouse Model

EQ101 is more effective than ruxolitinib (ruxo) at hair regrowth and suppression of cytotoxic CD8+ T-cells in humanized alopecia model

EQ101 Improves Hair Regrowth



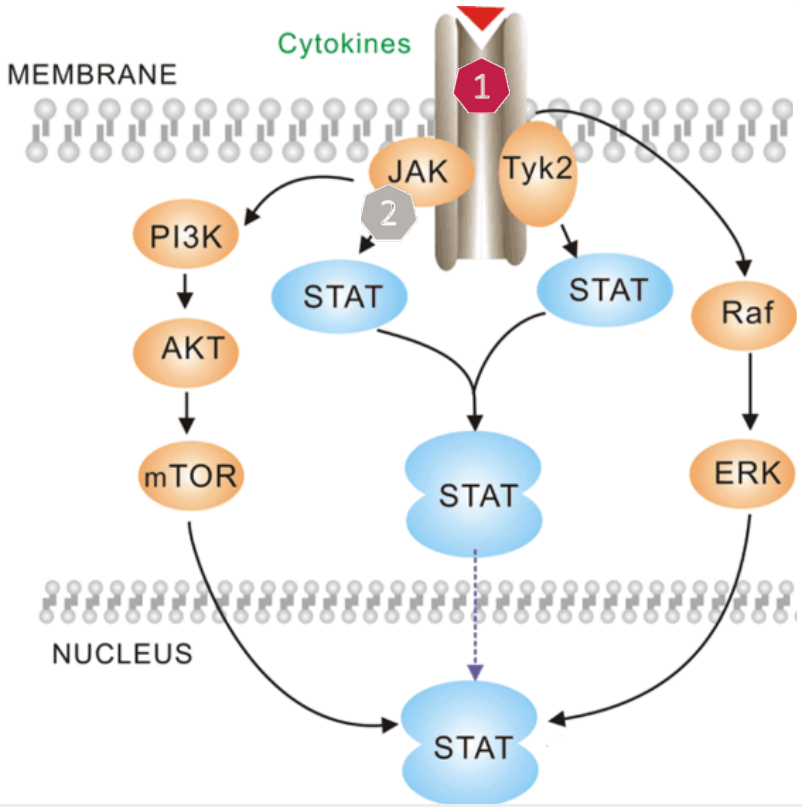
EQ101 Reduces CD8+ Cytotoxic T-cell Activation Marker



In-house data and Frohna *et al.*, Alopecia Areata Research Summit 2018

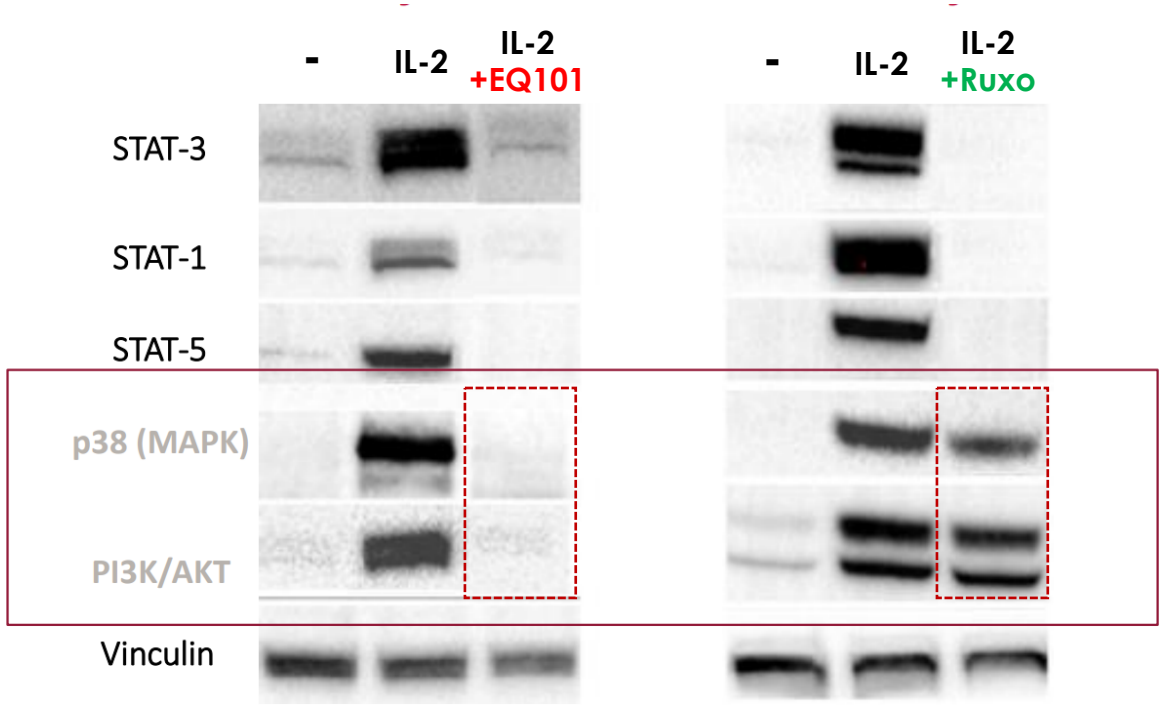
EQ101 Provides Complete Cytokine-mediated Signal Inhibition

JAKi effect on cytokine signaling is broad yet incomplete, whereas EQ101 can inhibit multiple downstream pathways for a more potent suppression of cytokine signaling



1 EQ101

2 JAKi



In-house data and Frohna et al., Alopecia Areata Research Summit 2018

EQ101: Alopecia Areata

Prioritizing Phase 2 in alopecia areata with potential to target multiple follow-on indications with significant unmet medical need

Strong biologic rationale

- Potent and selective inhibition of IL-2, IL-9 and IL-15 – cytokines important to disease pathogenesis
- Strong response in inhibiting immune-mediated hair loss in a humanized mouse model

Planned Phase 2 in Alopecia areata

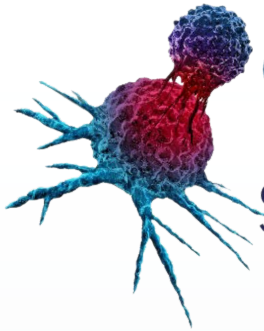
- IND open for Phase 2 study
- Plans to initiate POC trial in 2H of 2022

Attractive commercial opportunity

- 300,000 moderate to severe patients in U.S. – only one approval (Olumiant)
- JAK inhibitors validate target biology, but may be limited by class safety concerns
- Enthusiasm for novel, non-JAK inhibitor approach

Acknowledgments & Q&A

- Bioniz Research Team (past & present
- NIH Research Teams
- Dr. Nazli Azimi (co-founder)
- Professor Yutaka Tagaya (co-founder)
- Equillium Research Team
- Patients of the clinical trials
- KOLs and advisors
- Our investors



Cytokine Based Drug Development Summit

BIONIZ THERAPEUTICS

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