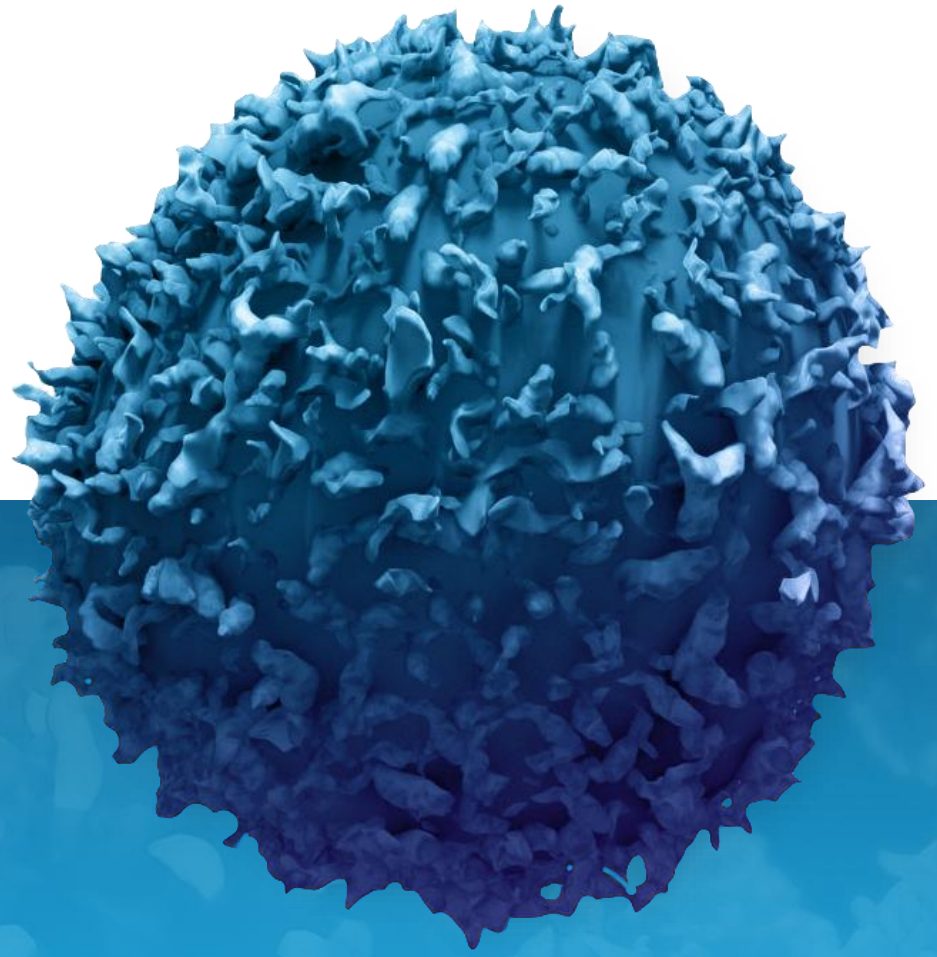

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Corporate Presentation

February 2024

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Equillium: Investment Highlights

Anticipated Milestones

- Phase 3 aGVHD topline data – Q1 2025

Commercial Rights to Itolizumab

- Full commercial rights to all indications
- EQ Territories: US, Canada, Australia & New Zealand

Itolizumab Derisked

- IDMC recommends Phase 3 EQUATOR study in aGVHD proceed as planned
- Positive topline Phase 2 UC data
- Positive topline Phase 1b aGVHD data
- Positive topline Phase 1b LN data
- Commercial-scale manufacturing in place w/ Biocon

Attractive Market Opportunities

- **GVHD:** No drugs approved in 1L aGVHD
- **GVHD:** Approved drugs approaching $1B in US sales
- **GVHD:** Potential to market independently with small commercial team
- **UC:** Unmet medical need for novel / complementary mechanisms

Additional Opportunities: Multi-cytokine Inhibitors

- EQ101: IL-2/9/15 inhibitor
  Alopecia Areata – Positive Phase 2 data reported
  Cutaneous T Cell Lymphoma – clinical POC demonstrated
- EQ302: Oral IL-15/21 inhibitor
  Preclinical stage, targeting gastrointestinal indications

Abbreviations: aGVHD, acute graft-versus-host disease; cGVHD, chronic graft-versus-host disease; IDMC, independent data monitoring committee; UC, ulcerative colitis; LN, lupus nephritis; 1L, first-line; 2L, second-line

Diversified Pipeline of Differentiated Immunology Assets

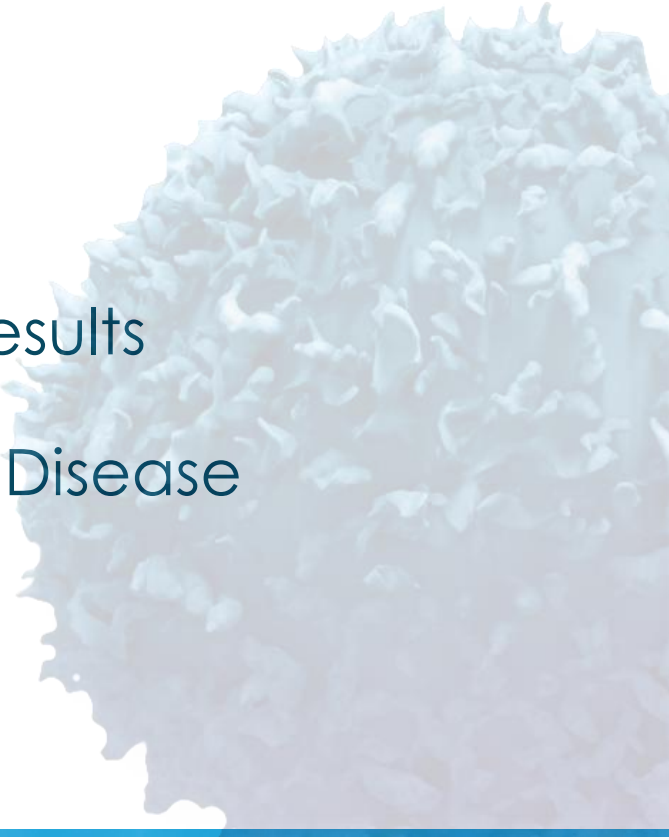
	Indication	Pre-Clinical Phase 1 Phase 2 Phase 3	Rights	Status
EQ001 itolizumab anti-CD6	**acute graft-versus-host disease**	FDA Fast Track & Orphan Drug Designations	equillium **US, CAN, AUS & NZ**	**Topline Phase 3 data anticipated Q1 2025**
	systemic lupus erythematosus (SLE) / lupus nephritis (LN)	FDA Fast Track Designation for LN		Positive PoC data announced April 2024
	ulcerative colitis	Co-sponsored with Biocon	Biocon **EU / Japan**	Positive Phase 2 data announced February 2025
EQ101 IL-2/9/15 inhibitor	**alopecia areata / CTCL** *(intravenously delivered peptide)*	PoC data & FDA/EMA Orphan Drug Designations for CTCL	equillium	Activities on hold pending additional resources
EQ302 IL-15/21 inhibitor	**gastrointestinal indications** *(orally delivered peptide)*			Activities on hold pending additional resources

Abbreviations: SLE, Systemic lupus erythematosus; LN, lupus nephritis; PoC, proof-of-concept; CTCL, Cutaneous T-cell lymphoma

Itolizumab

First-in-Class immune-modifying mAb targeting the CD6-ALCAM signaling pathway

- Mechanism of Action
- Safety Data & Clinical Results
- Acute Graft-Versus-Host Disease
- Ulcerative Colitis



CD6-ALCAM Pathway is Central to Immuno-Inflammation

CD6 is a **co-stimulatory receptor overexpressed on T_{eff}** and down-regulated on T_{reg}

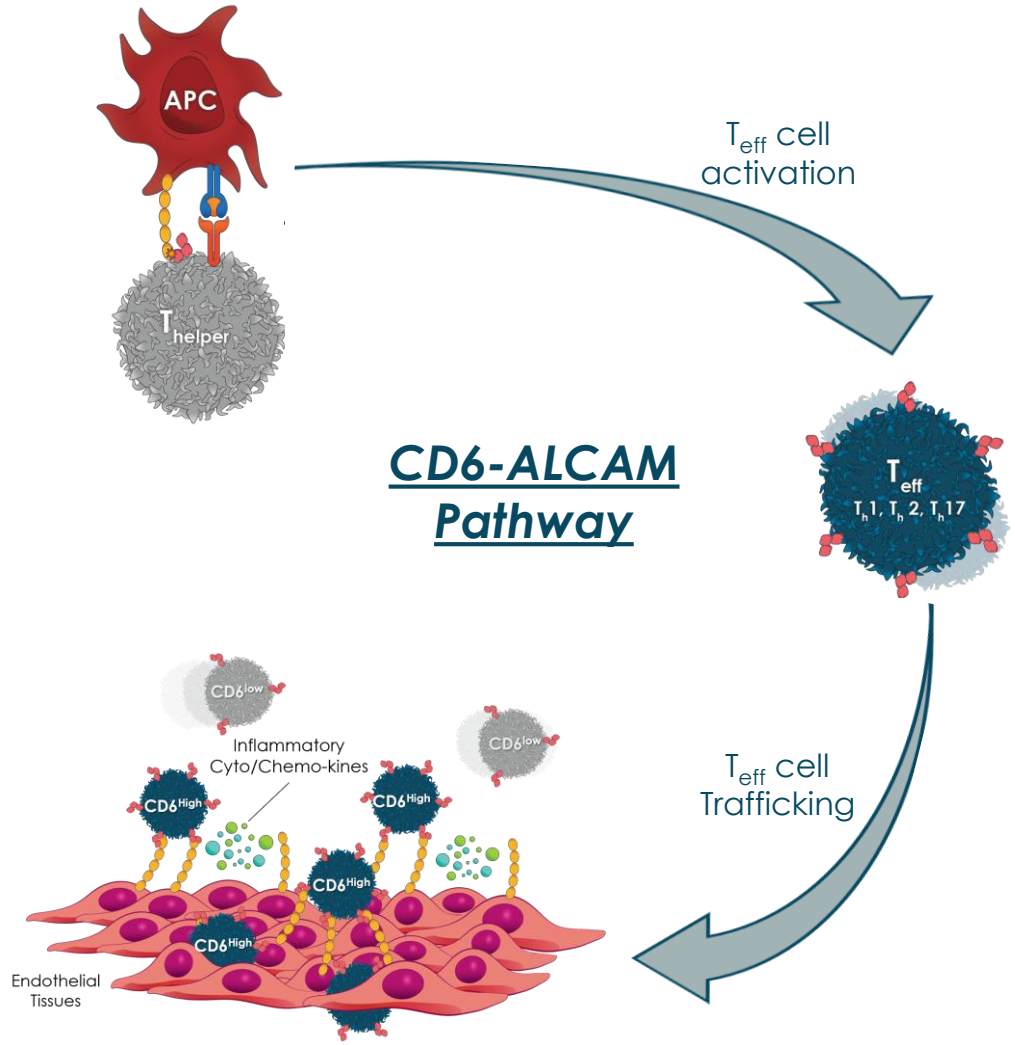
$CD6^{High}$ cells exhibit greater pathogenic capacity

Activated leukocyte cell adhesion molecule (ALCAM), is expressed on both antigen-presenting cells and tissues including BBB, skin, gut, lung, liver and kidney

The binding of CD6-ALCAM is important for:

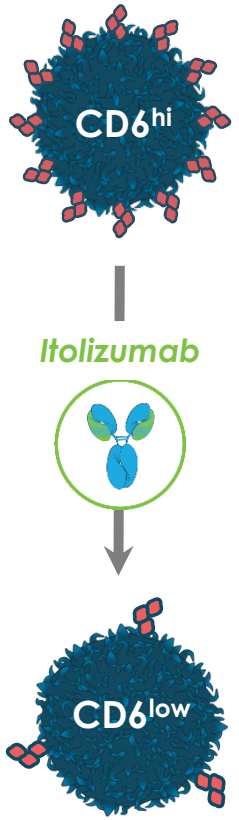
- Immune **synapse formation**
- Optimal **co-stimulation and activation of T_{eff}**
- **Trafficking** into tissues

The **CD6-ALCAM pathway modulates T cell activity and trafficking** central to the pathogenesis of multiple immuno-inflammatory diseases



Cytokines reduces Including but not limited to IFN-γ, TNF-a, IL-4, IL-5, IL-6, IL-13 and IL-17. Consuegra-Fernandez et al., Cellular & Molecular Immunology 2018; Ma et al., Journal of Crohn's and Colitis 2019
Abbreviations: ALCAM, activated leukocyte cell adhesion molecule; BBB, blood brain barrier

Itolizumab-induced Loss of Cell Surface CD6 Inhibits T_{eff} Cells

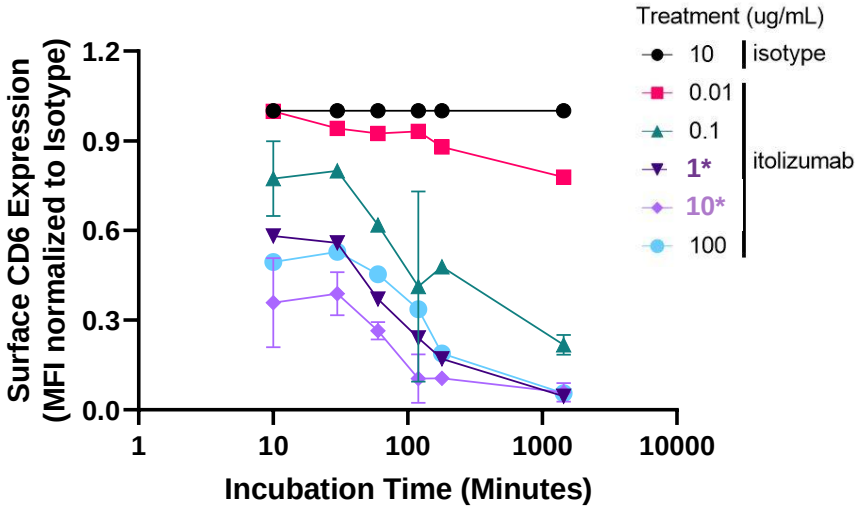


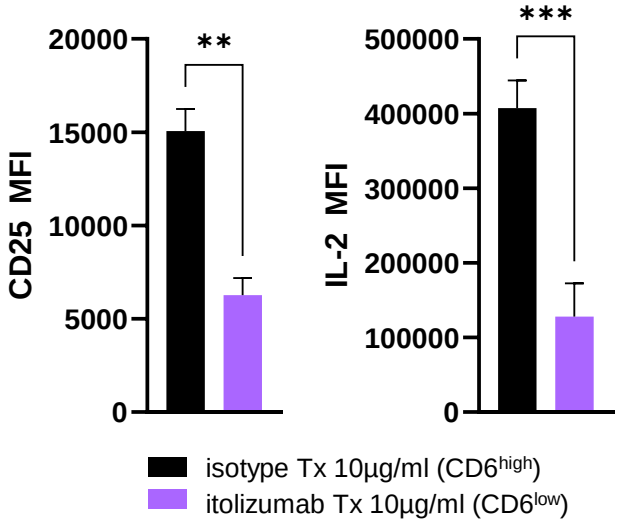
Pathogenic T_{eff} Cells

Antigenic Modulation (shedding)

Non-pathogenic T_{eff} Cells

Itolizumab leads to loss of CD6 in both a dose and time-dependent manner resulting in T cells that are hyporesponsive to TCR stimulation†





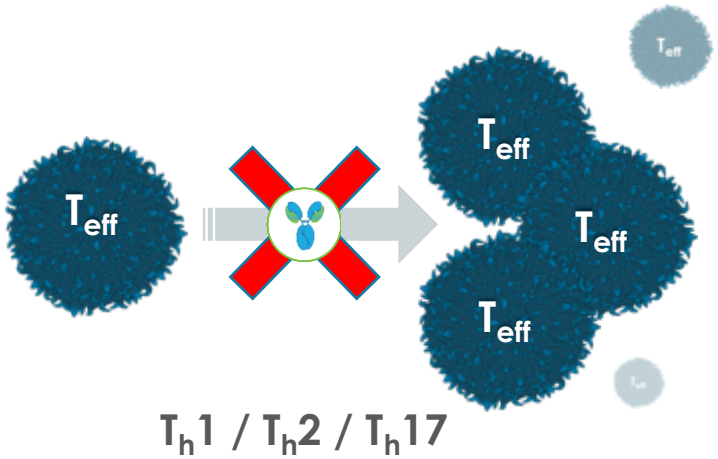
- Itolizumab binds to domain-1 of CD6 causing dose-dependent loss of CD6^
- Itolizumab-induced loss of CD6 results in hyporesponsive T cells
- Loss of CD6 is a pharmacodynamic marker that can be monitored in patients^

†Chu, D., Ampudia, J., Connelly, S., & Ng, C. (2021). American Association of Immunologists 104th annual meeting. See Equillium website for details.
**clinically relevant doses, **p<0.01, ***p<0.001*
^detected with a non-competing anti-CD6 antibody
Abbreviations: TCR, T-cell receptor

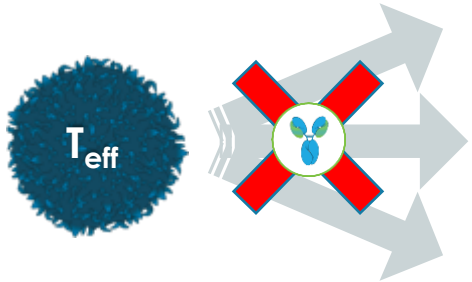
A Differentiated Approach to Treating Immuno-Inflammatory Disease

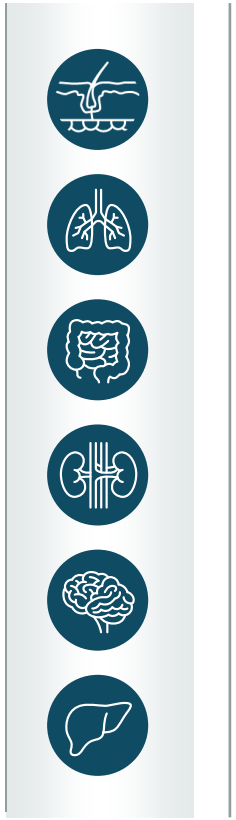
Selectively targets auto-reactive effector T cells, while sparing regulatory T cells to promote immune tolerance and homeostasis, resulting in durable disease remission

Synergistic inhibition of multiple T_{eff} cells and cytokines*

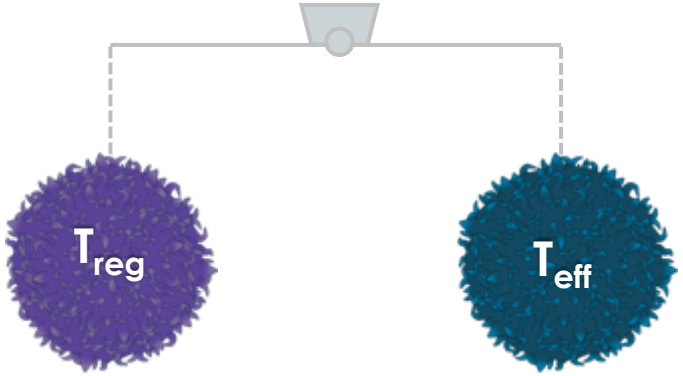


Inhibition of T_{eff} trafficking into key target organs



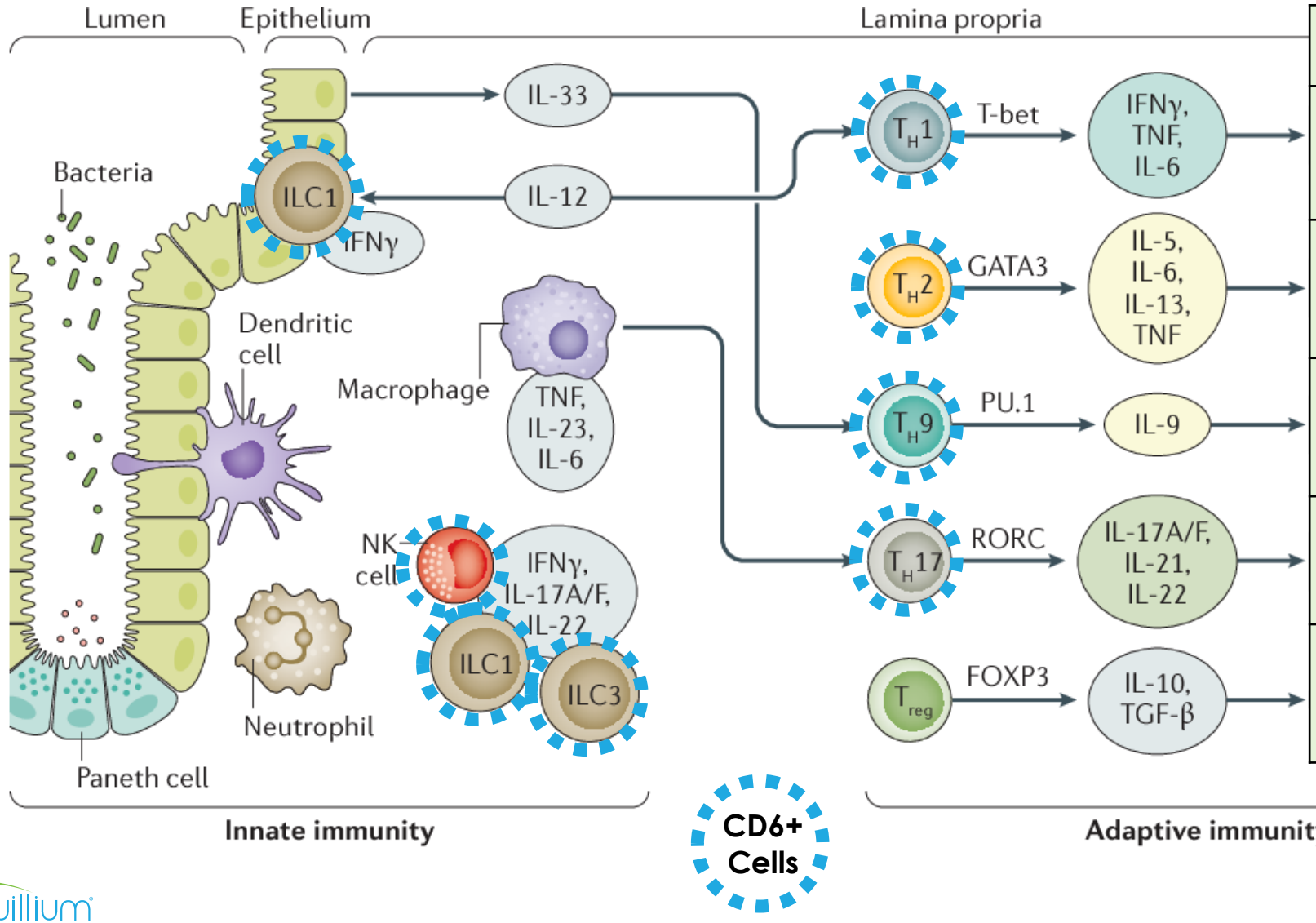


Restoration of immune regulation without broad immunosuppression



** including but not limited to IFN-γ, TNF-α, IL-4, IL-5, IL-6, IL-13 & IL-17*

CD6 Expressed on Multiple Effector Cells in GI Inflammation



aGVHD	ICI-Colitis	Crohn's Disease	Ulcerative Colitis
√	√	√	√
			√
	√		√
√	√	√	√
Disease Prevention/Resolution			

CD6-ALCAM Pathway Elevated in GI Inflammation

Journal of Crohn's and Colitis, 2019, 510–524
doi:10.1093/ecco-jcc/jjy179
Advance Access publication November 03, 2018
Original Article

OXFORD

JCC JOURNAL of CROHN'S and COLITIS

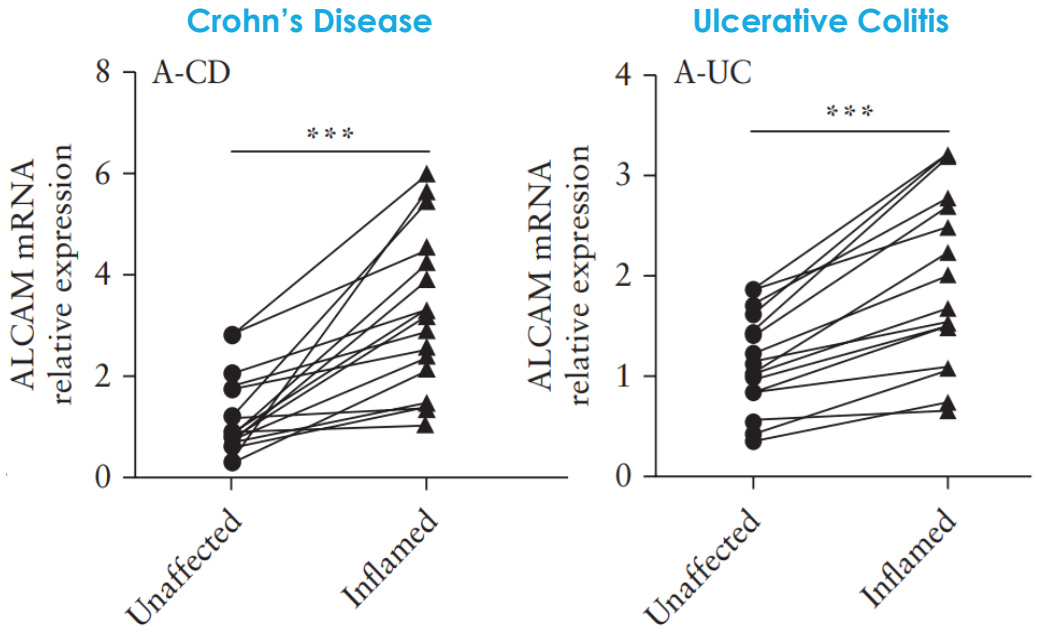
Original Article

Critical Role of CD6^{high}CD4^{+} T Cells in Driving Th1/Th17 Cell Immune Responses and Mucosal Inflammation in IBD

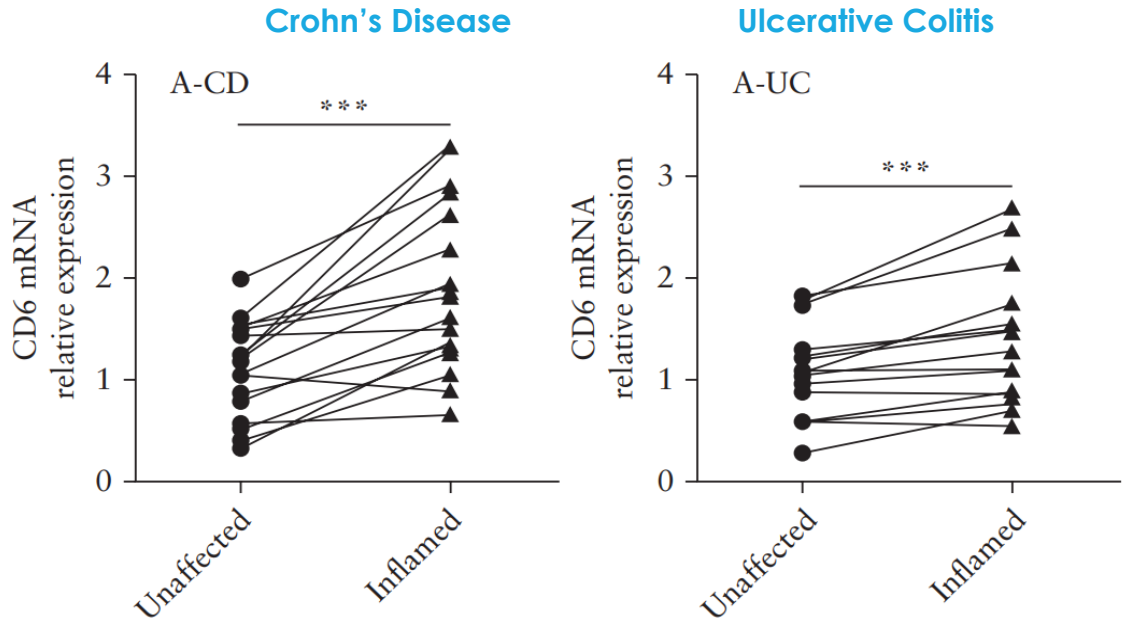
CD6^{high} Cells are Enriched in Inflamed GI Tissues

Increased ALCAM expression localized to inflamed tissue of IBD patients leading to increased infiltration and enrichment of CD6high Teff cells

ALCAM



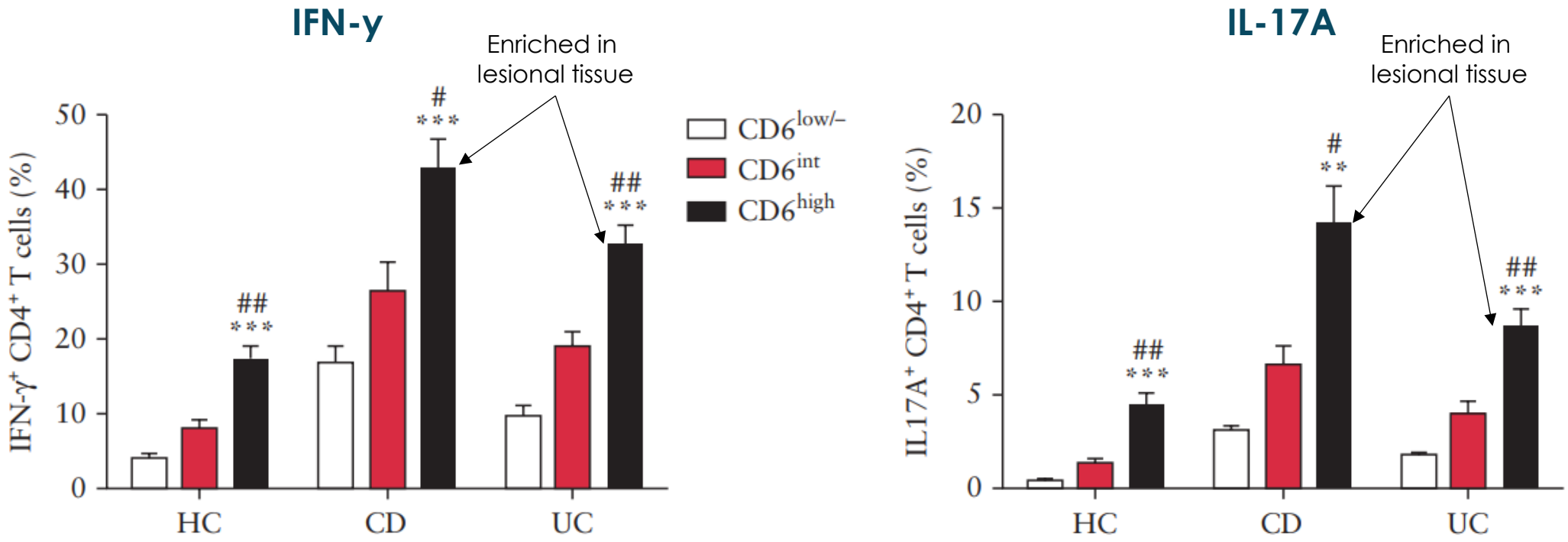
CD6



*Ma et al., J Crohns Colitis 2019. **p < 0.01, and ***p < 0.001 ****p < 0.0001*

Increased IFN-γ/IL-17 Secretion Associated with CD6^{high} Cells

Pathogenic dual IFN-γ / IL-17 expressing Th17 cells implicated in multiple autoimmune and inflammatory diseases are associated with levels of CD6 in IBD patients



*Ma et al., J Crohns Colitis 2019. **p < 0.01, and ***p < 0.001 ****p < 0.0001 versus CD6$^{low/-}$ group. #p < 0.05, and ##p < 0.01 versus CD6^{int} group. Data are shown as mean ± SEM*

Itolizumab: Critical Mass of Safety Data and Positive Clinical Results

Over 1,000 subjects dosed with itolizumab across numerous clinical studies

EQUATOR

Acute GVHD - Pivotal Phase 3 (ongoing)
IDMC Interim Review @ 100 patients in July 2024; recommended study should proceed

EQUATE

Acute GVHD - Phase 1b (completed)
Study demonstrated high rates of rapid and durable complete response

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equalise

Lupus nephritis - Phase 1b (completed)
Study demonstrated clinically meaningful responses in highly proteinuric subjects

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Ulcerative colitis - Phase 2 (Completed)
Study demonstrated clinical efficacy after 12 weeks of treatment

Additional Biocon Studies

- Healthy volunteers
- Rheumatoid arthritis
- Psoriasis (approved in India)
- COVID-19 CRS (approved EUA in India)

Biocon

Abbreviations: GVHD, graft-versus-host disease; IDMC, independent data monitoring committee; CRS, cytokine release syndrome, EUA, emergency use authorization

Itolizumab in GVHD: Executive Summary

- Positive topline data from Phase 1b EQUATE study in acute graft-versus-host disease
  - Achieved CR and ORR at Day 29 of 48% and 65%, respectively*
  - Response at Day 29 was associated with improved progression-free survival through 1 year
  - Responders were able to taper steroids by 70% at Day 29 and 99% at Day 169
  - Itolizumab continued to demonstrate favorable safety, tolerability and efficacy profile
- **A positive data result from Phase 3 EQUATOR study is expected to support registration**
- **Currently no drugs approved for first-line aGVHD**
- **Commercial scale manufacturing in place (Biocon)**
- Significant market: 2021 *JAMA Oncology* study estimated ~10,000 patients receive allo-HSCT annually
  - ~ 20-40% of HSCT patients develop acute GVHD**
  - ~ 40-50% develop chronic GVHD**
  - Approved therapies in 2L aGVHD & 2L cGVHD approaching $1 billion in revenue
- Attractive commercial opportunity: ability to launch independently with small commercial team
- Opportunities for rapid indication expansion through single Phase 3 studies

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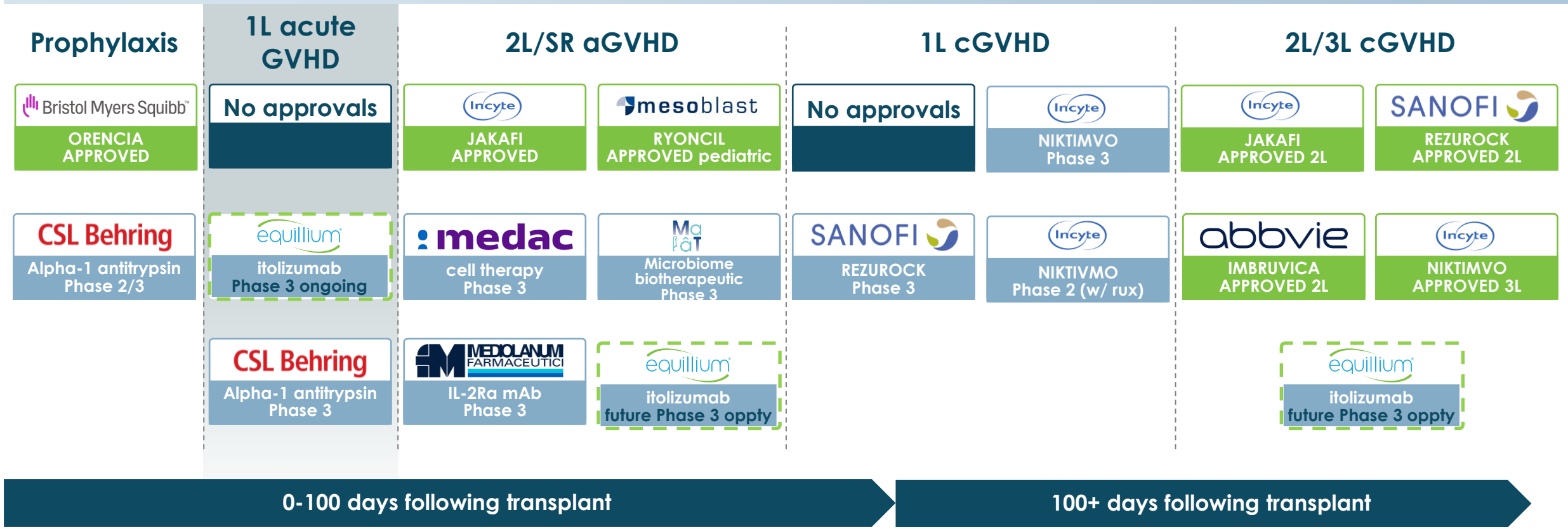
** All subjects dosed within 72 hours of corticosteroid administration*
*** 2022 Dana-Farber Report*
Abbreviations: CR, complete response rate; ORR, overall response rate; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplant

GVHD Competitive Landscape

Growing strategic interest in GVHD with recently demonstrated market potential:

JAKAFI: US sales in SR-aGVHD and 2L cGVHD estimated at **$500M**

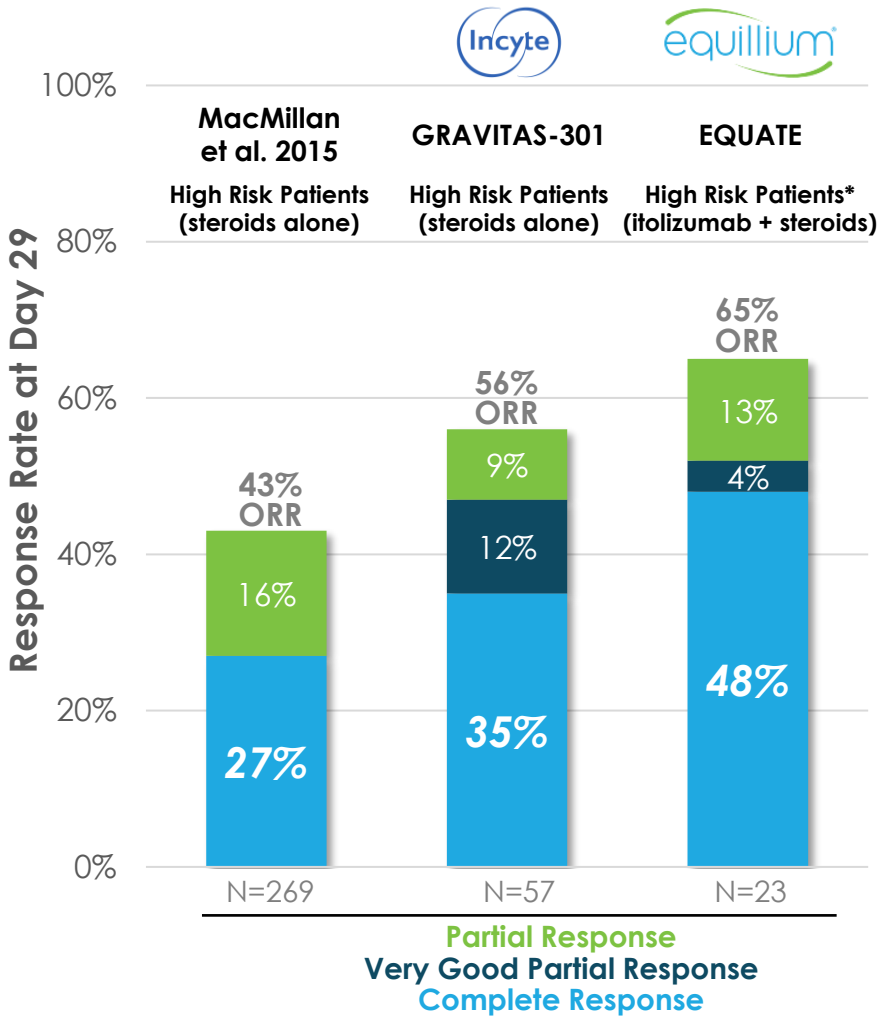
REZUROCK: US sales in 2L cGVHD estimated at **$425M**, ~3 years into launch (acquired by Sanofi $1.9B in 2021)



2024 revenue estimates, sources Evaluate Pharma & Incyte report, July 2024

Abbreviations: SR-aGVHD, steroid refractory acute graft-versus-host disease; cGVHD, chronic graft-versus-host disease; 1L, first-line; 2L, second-line; 3L, third-line

Standard of Care: High-Dose Steroids Achieve Poor CR Outcomes



Steroids alone yield poor Complete Response rates in high-risk aGVHD

Complete Responses are associated with improved long-term clinical outcomes

Clinicians indicate a 10% improvement in Complete Response rate is clinically meaningful

EQUATE

Phase 1b open label, dose escalation study of itolizumab in patients with high risk aGVHD

- **48% of patients on itolizumab (all dose levels) achieved Complete Response** at Day 29 when dosed within 72 hours of steroids
- Early responses allowed for **rapid steroid tapering – 70% at Day 29**
- Adverse events, including SAEs, are consistent with high-risk aGVHD population
- **74% of Day 29 Responders survived one year** across treatment groups ¥

** EQUATE high-risk is defined as Grade III-IV by MAGIC criteria and Grade II with Ann Arbor Score of 2 or 3; 70% of subjects also met Minnesota high-risk criteria used by MacMillan and GRAVITAS-301; EQUATE data shown for subjects dosed with 72 hours of steroid administration.*

¥ Subjects with a PR, VGPR, or CR at Day 29 were considered Day 29 Responders; final data (database lock with cut-off date of 15 Dec 2022).

Abbreviations: ORR=CR+VGPR+PR, ORR = overall response rate; PR = partial response; CR = complete response; VGPR = very good partial response defined as achieving all the criteria for skin, liver, and gut involvement per Martin 2009 Consensus criteria without meeting the criteria for CR. MacMillan et al. BBMT 2015; Zeiser et al. Lancet Hematology 2022.

EQUATOR Study: First-line Treatment of High-Risk aGVHD

EQUATOR

Over 35 US clinical sites active, including 9 of top 10 U.S. allogeneic HSCT centers

High exposure of itolizumab to key hospital systems and KOLs

Phase 3 randomized, double-blind, global pivotal study of itolizumab in ~ 200 patients

John Koreth, MD, Dana-Farber Cancer Institute, Principal Investigator

Eligible Patients: Grade III-IV & Grade II with lower GI

Dosing: concomitant within 72 hours of high-dose corticosteroid treatment (2 mg/kg)

R

Itolizumab:
IV 1.6 mg/kg loading dose followed by 0.8 mg/kg Q2W x 6 doses (n=100)

Steroid tapering recommendation

Placebo:
(n=100)

Day 1 | Day 15 | **Day 29** | Day 43 | Day 57 | Day 71 | Day 85

Dosing Schedule: patients followed out to Day 365

Primary Outcome
- **Complete Response at Day 29**

Key Secondary Outcomes
- **Durability of Complete Response from Day 29 through Day 99**
- **ORR at Day 29**

Interim IDMC review @ 100 patients
- Futility and efficacy
- Completed 31 July 2024
- Result: study should proceed

Planned acceleration to complete study
- ~ 155 patients enrolled

Abbreviations: aGVHD, acute graft-versus-host disease; GI, gastrointestinal; HSCT, hematopoietic stem cell transplant; KOL, key opinion leader

Itolizumab in Ulcerative Colitis: Demonstrated Clinical Efficacy

Strong mechanistic rationale in GI disease

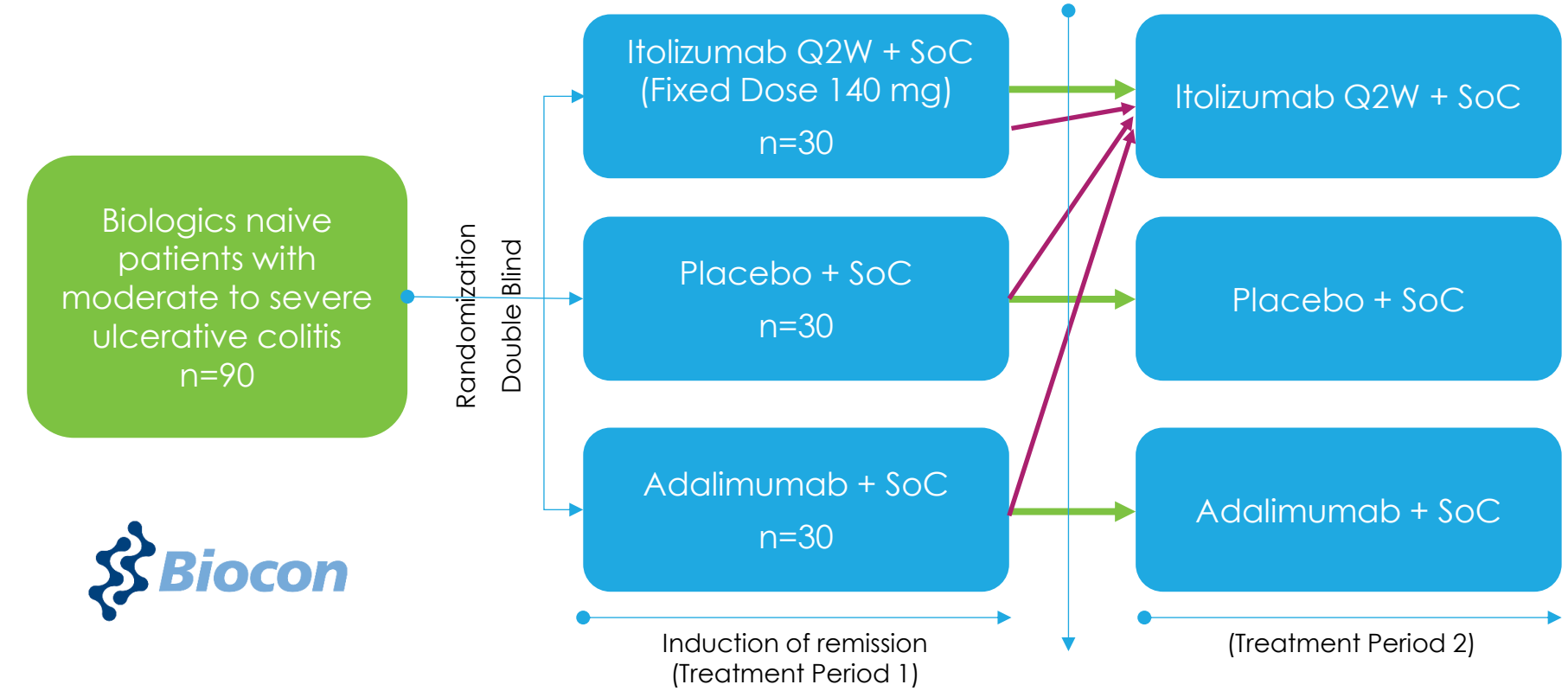
- $CD6^{high}$ T_{eff} cells have greater pathogenic potential and are associated with GI inflammation
- The CD6-ALCAM pathway is upregulated in inflammatory lesions of patients with GI inflammation and correlates with disease severity
- Itolizumab shown to be effective in treating GI inflammation in multiple models of GI disease

Phase 2 clinical data (n=90)

- Itolizumab vs. placebo vs. adalimumab
- **Primary Endpoint:** clinical remission rate at 12 weeks was 23% on itolizumab vs. 20% on adalimumab* vs.10% on placebo
- **Key Secondary Endpoint:** endoscopic remission at 12 weeks was 16.7% on itolizumab vs. 16.7% on adalimumab s. 6.7% on placebo
- Itolizumab was generally well tolerated, consistent with prior clinical experience

** One patient from the adalimumab arm had endoscopic remission, but was recorded as not in clinical remission at week 12 due to missing sub-score data;*
Abbreviations: GI, gastrointestinal

UC Phase 2 Study – Conducted by Biocon in India



Primary endpoint:
Proportion of subjects who achieved clinical remission per Total Mayo Score at Week 12

Endoscopy at screening, week 12 and week 24 (central endoscopy)

Abbreviations: Q2W, once every two weeks; EoS, end of study; EoT, end of therapy; SOC, standard of care
Standard of care: oral medications prednisone, azathioprine or 6-mercaptopurine and 5-aminosalicylates; patients to be on stable dose 2-4 weeks prior to randomization and maintain stable dose during first treatment period
Total Mayo Score: rectal bleeding, stool frequency, physician assessment, and endoscopy appearance. Each rated 0 to 3, total score of 0 to 12
Clinical remission defined as Total Mayo Score ≤ 2 and no sub-score >1

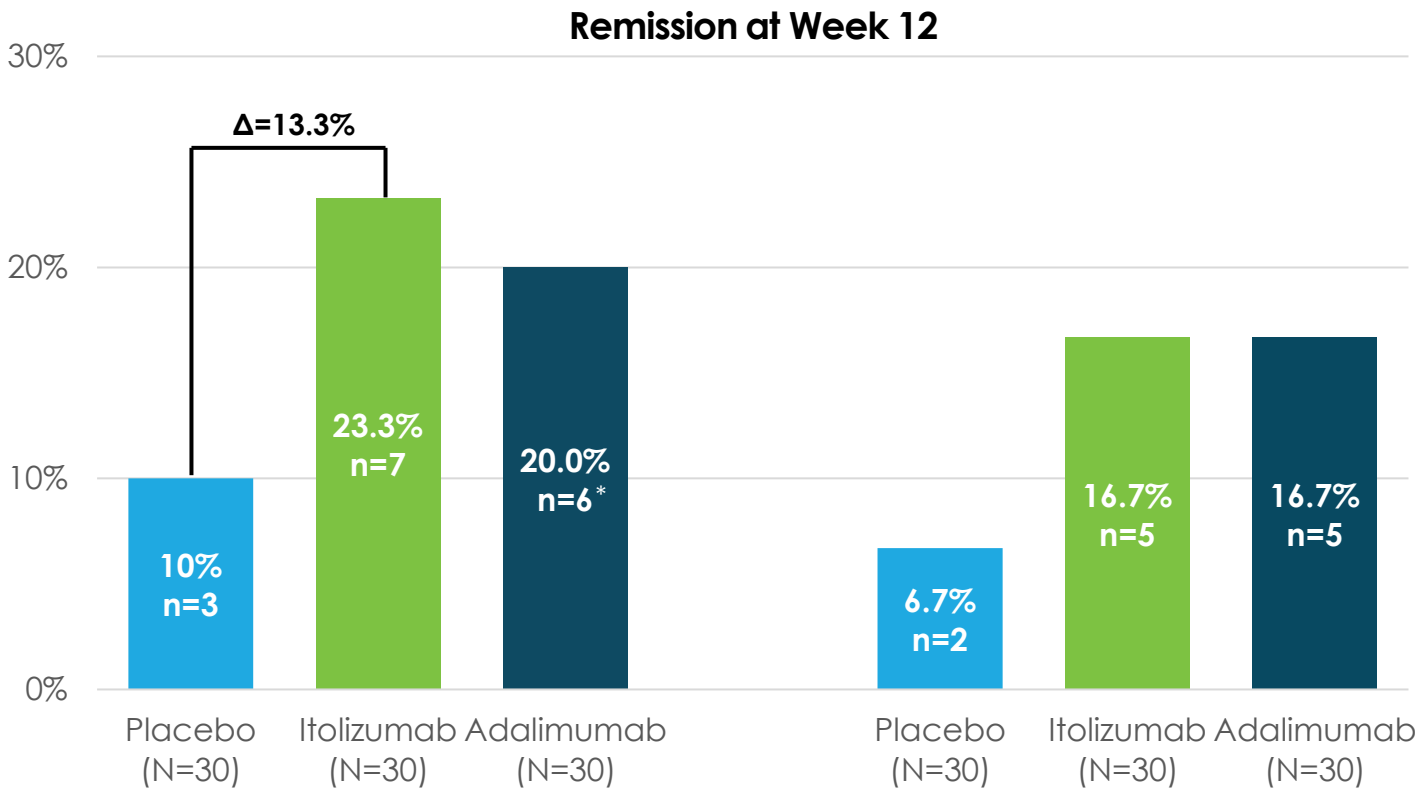
Baseline Demographics & Characteristics

DEMOGRAPHICS	Placebo (N=30)	Itolizumab (N=30)	Adalimumab (N=30)	Total (N=90)
Age (years), median (range)	38.5 (20-63)	38.0 (22-64)	43.5 (19-71)	39 (19-71)
Sex, n (%)				
Male	13 (43.3)	15 (50.0)	16 (53.3)	44 (48.9)
Female	17 (56.7)	15 (50.0)	14 (46.7)	46 (51.1)
Race - Asian, n (%)	30 (100)	30 (100)	30 (100)	90 (100)
Weight (kg), mean (SD)	60.2 (11.92)	55.9 (11.52)	58.0 (9.56)	58.0 (11.06)

CHACTERISTICS	Placebo (N=30)	Itolizumab (N=30)	Adalimumab (N=30)	Total (N=90)
Ulcerative Colitis Type, n (%)				
Proctosigmoiditis	8 (26.7)	5 (16.7)	8 (26.7)	21 (23.3)
Left sided colitis	15 (30.0)	20 (66.7)	13 (43.3)	48 (53.3)
Pancolitis	7 (23.3)	5 (16.7)	9 (30.0)	21 (23.3)
Ulcerative Colitis Disease Severity, n (%)				
Moderate (Total Mayo Score 6-10)	**30 (100)**	**23 (76.7)**	**30 (100)**	83 (92.2)
Severe (Total Mayo Score 11-12)	**0**	**7 (23.3)**	**0**	7 (7.8)
Total Mayo Score, median (range)	8.5 (6-10)	9 (6-11)	8 (6-10)	9 (6-11)
Central Endoscopy Score, n (%)				
2	**23 (76.7)**	**15 (50.0)**	**18 (60.0)**	56 (62.2)
3	**7 (23.3)**	**15 (50.0)**	**12 (40.0)**	34 (37.8)
Corticosteroid Use as SoC, n (%)	20 (66.7)	17 (56.7)	19 (63.3)	56 (62.2)
Azathioprine Use as SoC, n (%)	8 (26.7)	8 (26.7)	9 (30.0)	25 (27.8)

UC Phase 2 Study – Clinical & Endoscopic Remission Rates

Itolizumab achieved meaningful clinical remission rate despite an imbalance of more severe patients compared to placebo and adalimumab study arms



Clinical Remission
Total Mayo score of ≤ 2 and no individual sub-score greater than 1

Endoscopic Remission
Endoscopy sub-score=0

Adalimumab and placebo response rates consistent with prior studies

Itolizumab was generally well tolerated consistent with prior clinical experience

Potential read-through where lower gastrointestinal pathogenesis is a key driver of disease, e.g. GVHD

** One patient from the adalimumab arm had endoscopic remission, but was recorded as not in clinical remission at week 12 due to missing sub-score data*

Safety Overview – Treatment Period 1 (Week 0 -12)

	Placebo (N=30) n (%)	Itolizumab (N=30) n (%)	Adalimumab (N=30) n (%)	Total (N=90) n (%)
Patient with any TEAE	6 (20.0)	15 (50.0)	7 (23.3)	28 (31.1)
Patient with any ≥ Grade 3 TEAE	0	4 (13.3)	1 (3.3)	5 (5.6)
Patient with any related TEAE	0	10 (33.3)	2 (6.7)	12 (13.3)
Patient with any related ≥ Grade 3 TEAE	0	2 (6.7)	0	2 (2.2)
Patient with any serious TEAE	0	0	0	0
Patient with any TEAE leading to study drug discontinuation	0	0	0	0
Patient with any TEAE leading to death	0	0	0	0

- Both itolizumab related Grade 3 TEAEs are reductions in lymphocyte count – a known pharmacodynamic effect of itolizumab that has not been associated with increased risk of infection.
- Additional itolizumab Grade 3 TEAEs of anemia (also reported in adalimumab arm) and pyrexia (attributed to underlying disease) were considered not related to study drug.

Abbreviations: TEAE, treatment emergent adverse event
Topline data and subject to change

Corporate

Leadership

Intellectual Property

Financials & Milestones

Accomplished Executive Leadership

Bruce Steel, CFA
CHIEF EXECUTIVE OFFICER

BioMed Ventures • Rincon
Anaphore • Ambit

Steve Connelly, PhD
CHIEF SCIENTIFIC OFFICER

BioMed Ventures • aTyr Pharma
The Scripps Research Institute

Christine Zedelmayer
CHIEF OPERATING OFFICER

Amylin • Amgen • Ligand

Jason Keyes
CHIEF FINANCIAL OFFICER

Orexigen • Amylin
Amgen • Baxter

Joel Rothman
CHIEF DEVELOPMENT OFFICER

Cytokinetics • Genentech
Raptor • Jazz Pharmaceuticals

Matt Ritter, PhD
SVP CORPORATE DEVELOPMENT

La Jolla Pharmaceutical
EyeCyte • The Scripps
Research Institute

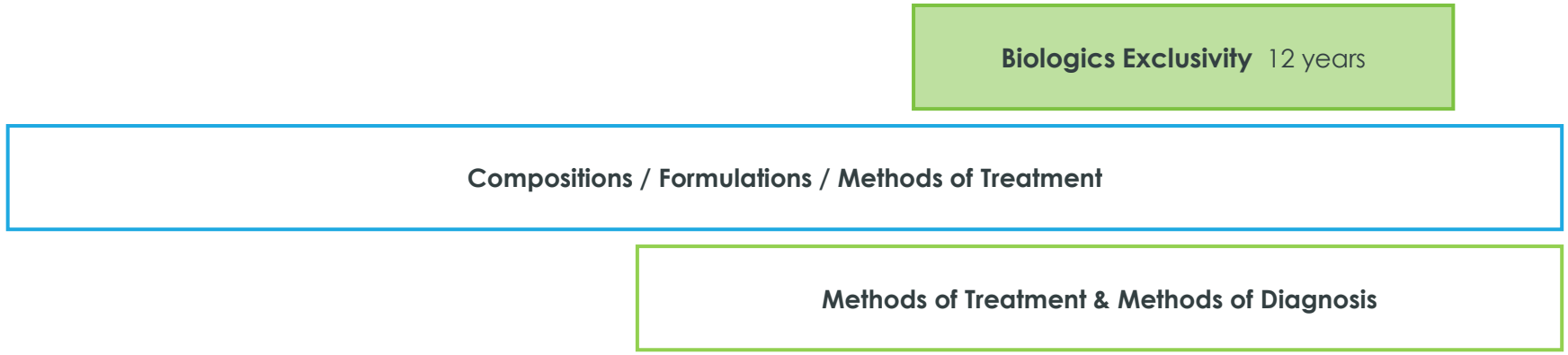
Extensive Industry Experience

AMYLIN · ambit · AMGEN · anaphore · aTyr · Baxter · BioMed Ventures · Cytokinetics · La Jolla Pharmaceutical
Genentech · Ligand · Jazz Pharmaceuticals · Orexigen · P&G · raptor pharmaceutical corp. · Rincon Pharmaceuticals · Scripps Research

Equillium Intellectual Property & Regulatory Exclusivity

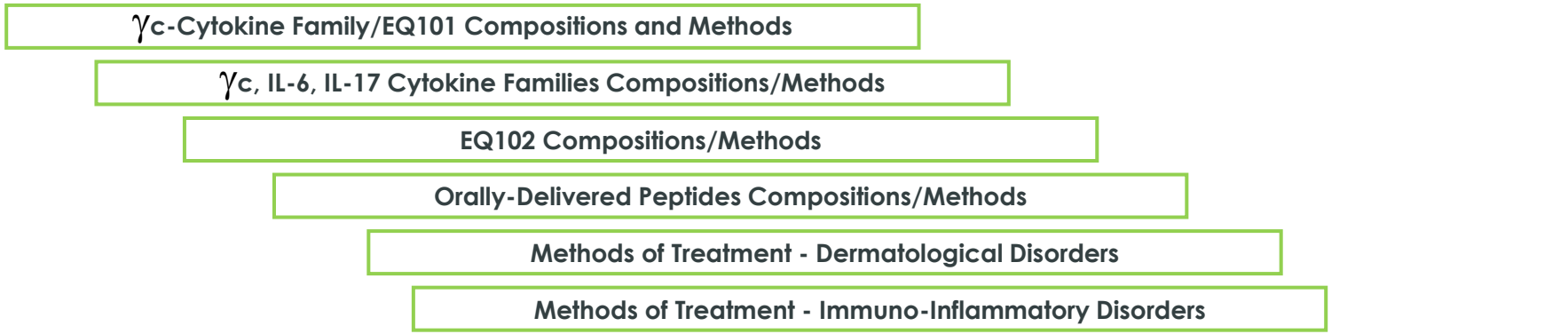
Itolizumab

12 patent families
26 issued patents
34 applications pending



Multi-Cytokine Technologies

6 patent families
98 issued patents
43 applications pending



Assumptions:
- Listed applications will issue
- Biologics Exclusivity will be granted and will begin at NDA approval
- Potential patent term extensions not shown

Itolizumab filings under exclusive license to Equillium for US, CA, AU, NZ
Cytokine Technologies are wholly owned and under prosecution in all major global markets
Patent and application counts as of August 2024

Equillium Financial Overview & Milestones

Key Financial Metrics

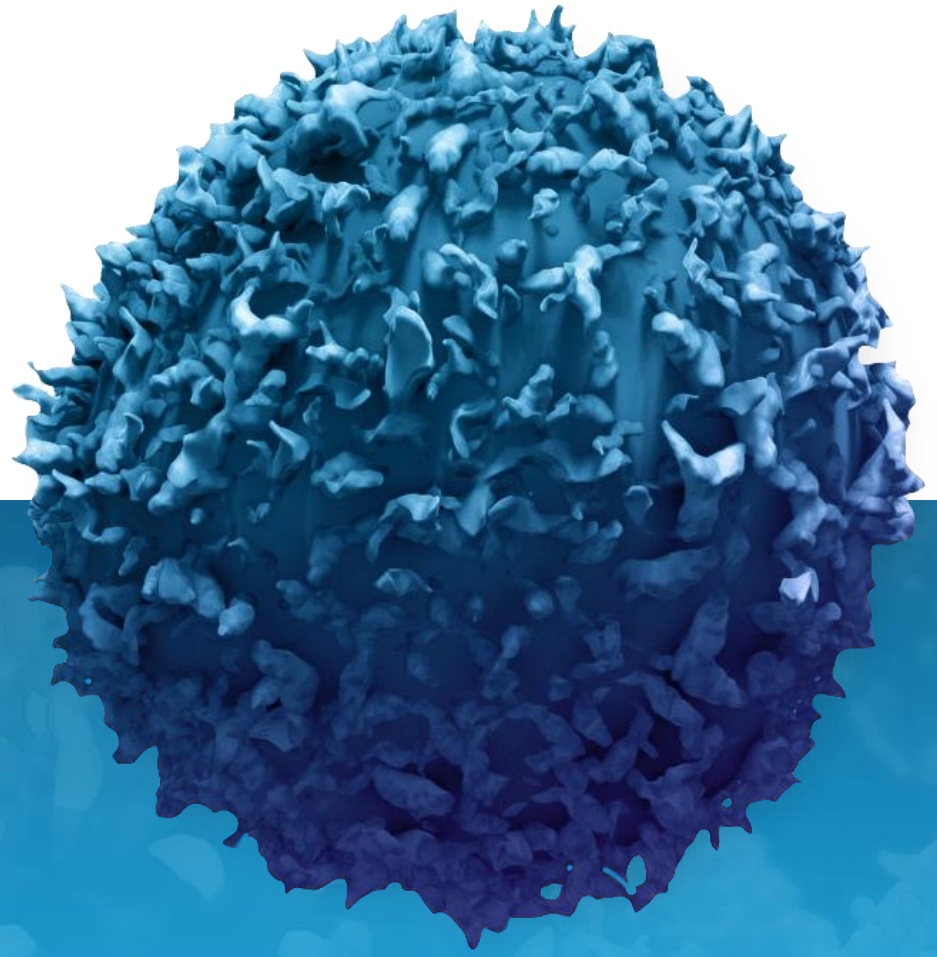
Total Cash and Investments (as of September 30, 2024)	$25.9 M
Q3 YTD 2024 Operating Burn	$15.7 M
Shares Outstanding (as of November 8, 2024)	35.4 M
Market Cap (as of close February 5, 2025)	$25.2 M

Please refer to the Form 10-Q filed on November 13, 2024 for complete financials of the company as of September 30, 2024

Equillium funded into Q4 2025*

Next milestone:
Phase 3 EQUATOR study topline data Q1 2025

* *Assuming acceleration of EQUATOR study completion to Q1 2025 and other operational adjustments*



equillium®

Thank you

www.equilliumbio.com

Appendix: *Multi-Cytokine Platform & Therapeutic Candidates*

Cytokine Challenge

Platform

MCi Advantage

EQ101 / EQ302

Cytokines are Validated Drug Targets

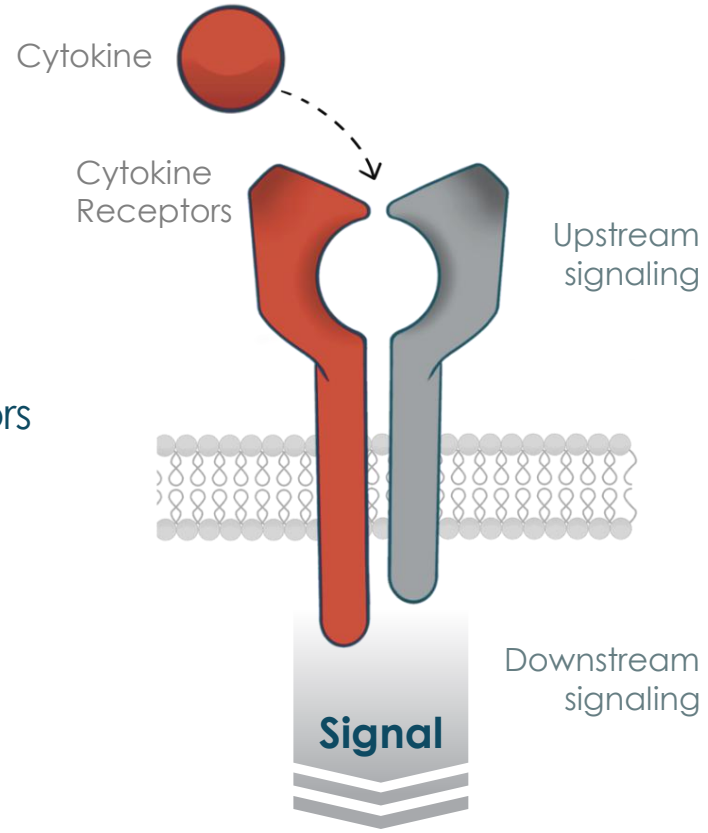
Cytokines are small signaling proteins with **essential roles in immune responses**, but when not properly regulated they are **key disease drivers**

Cytokines can exhibit overlapping or synergistic biological activities

Most drugs used to treat autoimmune and/or inflammatory diseases modulate cytokines by either:

1. *Directly neutralizing* cytokine binding to upstream receptors, such as anti-TNF
2. *Indirectly inhibiting* downstream cytokine signaling pathways, such as JAK inhibitors

Interleukins (IL) are a type of cytokine that play essential roles in the activation, proliferation and function of immune cells

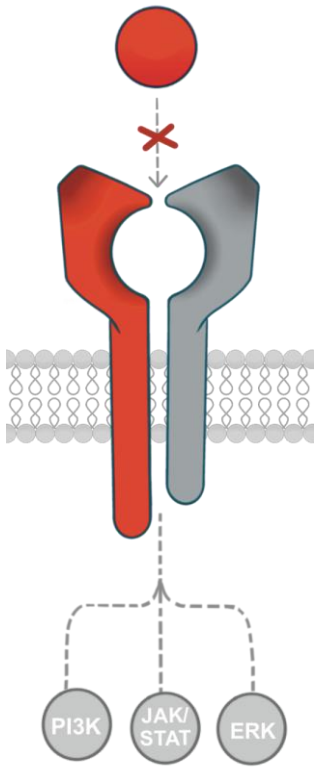


Challenges in Targeting Cytokine Signaling

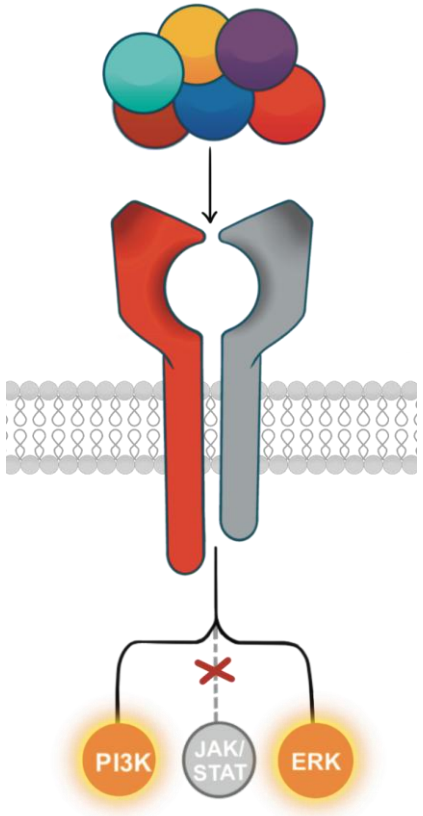
mAb
Inhibits Only One Cytokine

Upstream signaling

Downstream signaling



JAK inhibitor
Inhibits 50+ Cytokines



Ideal Therapeutic Approach
Selective inhibition of disease driving cytokines

Inhibiting the right combination of cytokines is key for optimal therapeutic effect, balancing both potent activity and potential toxicities

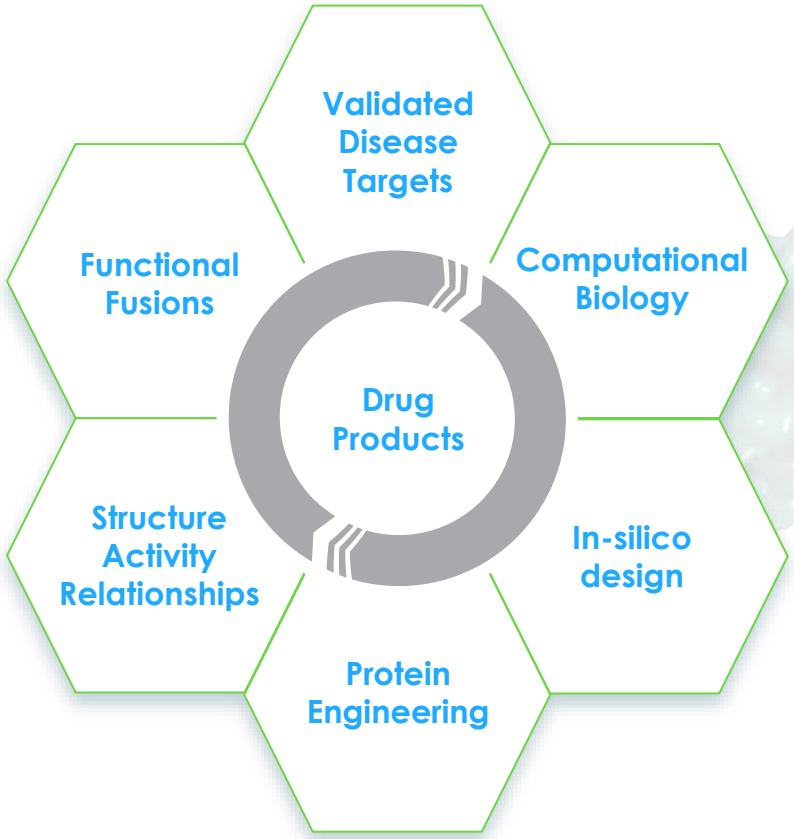
Inhibition too Narrow
Other Cytokines Involved, leads to insufficient activity

Inhibition too Broad
Non-selective cytokine targeting leads to broad immunosuppression and safety risks

Optimal Therapeutic Effect

Multi-Cytokine Inhibitor Platform

Modular platform generates products that **modulate the natural biological redundancy or synergy of cytokines** affording greater therapeutic benefit



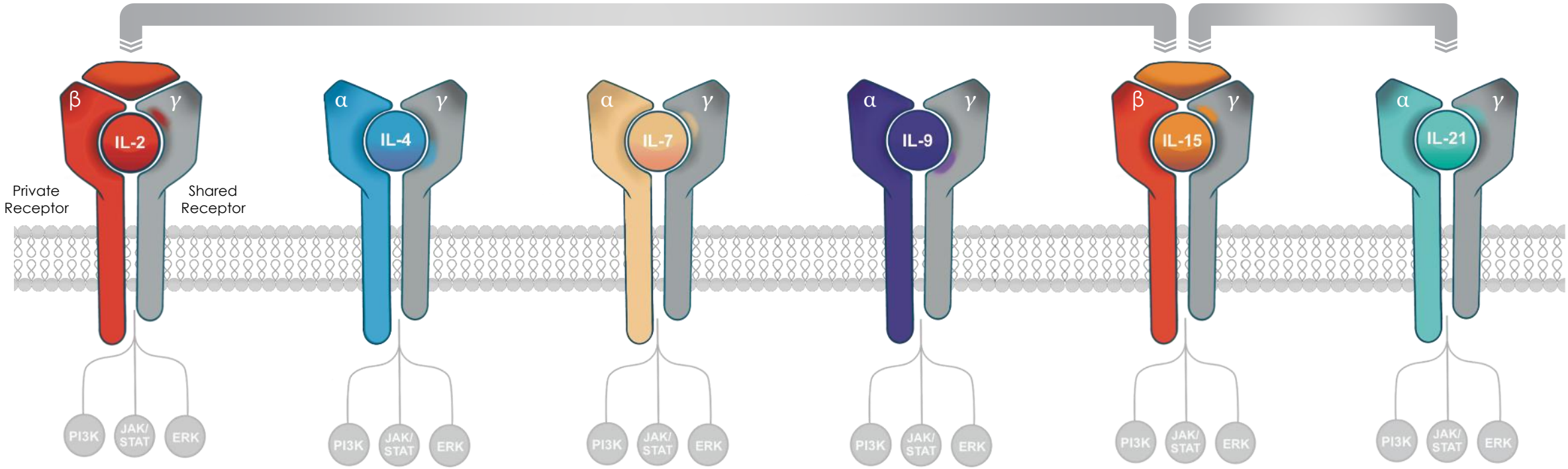
- Technology originating from the National Institutes of Health
- Uniquely targets upstream shared receptors to selectively modulate multiple cytokine pathways in a single novel product
- Intravenous, subcutaneous and oral delivery

- Products can be flexibly modified to optimize therapeutic profile and tissue targeting properties
- Broad IP portfolio covering the platform, methods of treatment and composition of matter

γC Receptor: A Key Shared Cytokine Signaling Hub

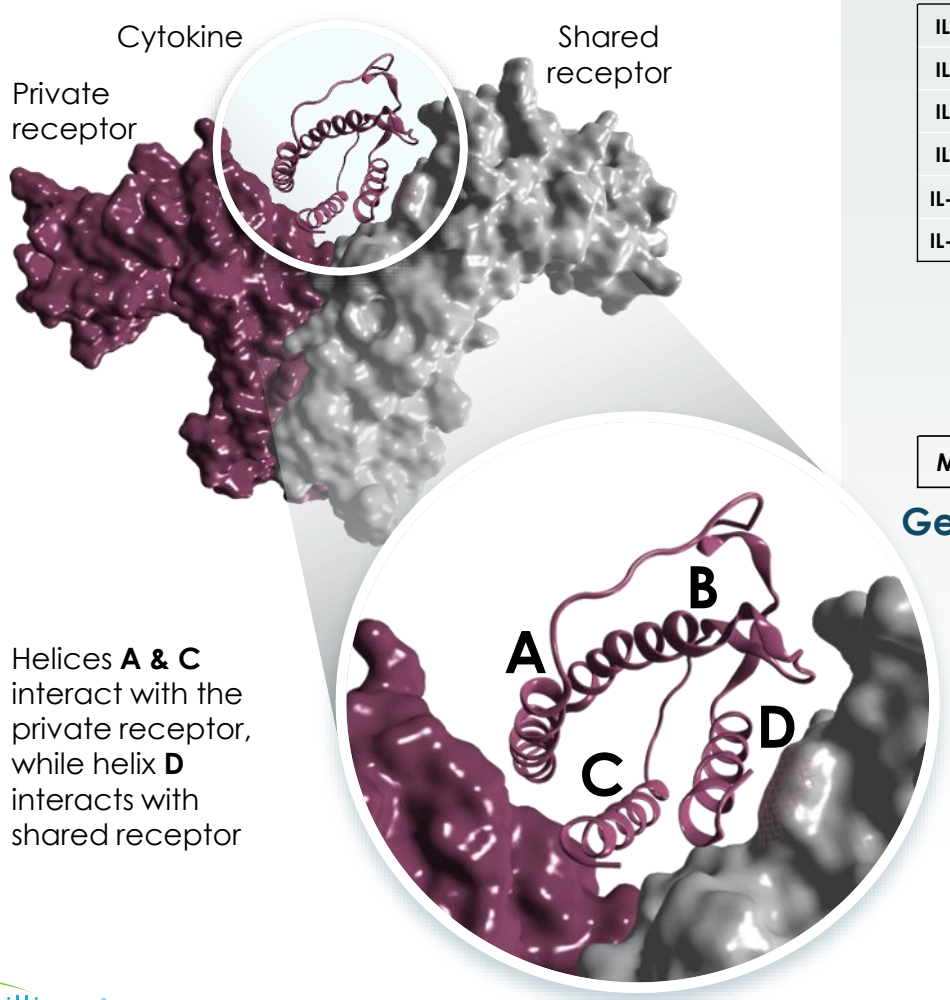
Cytokines of the γC receptor are critical regulators of immune responses
thus, making it an **attractive drug target** for modulating T, NK and B cells

Overlapping and synergistic signaling on CD4, CD8 & NK cytotoxic T cells



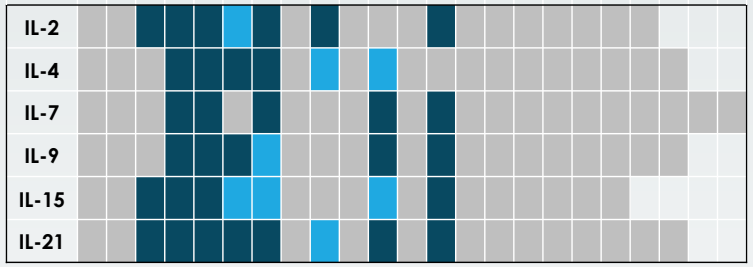
Generation of Selective Multi-Cytokine Inhibitors (MCi)

CYTOKINE-RECEPTOR COMPLEX



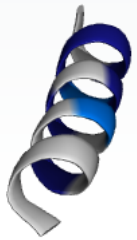
Helices **A & C** interact with the private receptor, while helix **D** interacts with shared receptor

CYTOKINE D-HELICES



Analyze native sequences

Generate proprietary composite sequence



Engineer multi-cytokine inhibitors

FUNCTIONAL MODIFICATIONS

PK extension strategies
PEGylation
Lipidation
FC-fused peptibodies

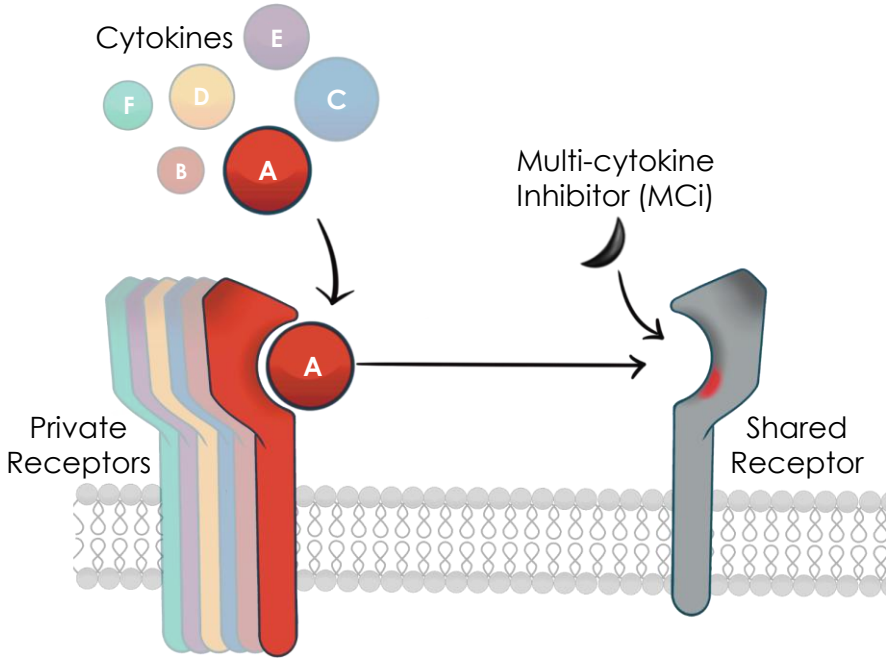
Proteolytic Stability
Non-natural amino acids
Peptide stapling

Multi-specific molecules
Fc-fusions – peptibodies
mAb-fusions – bi/tri-specific

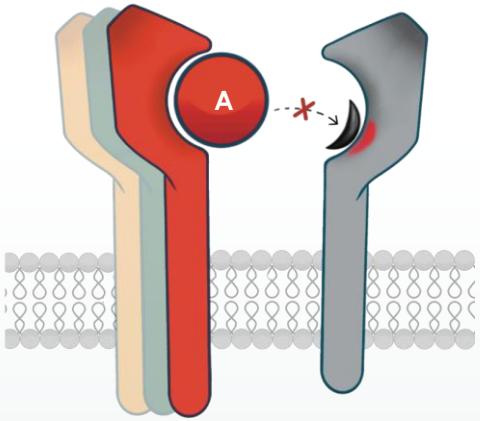
OPTIMIZED MCi THERAPEUTIC

Nata *et al*., J. Biol. Chem., 2015

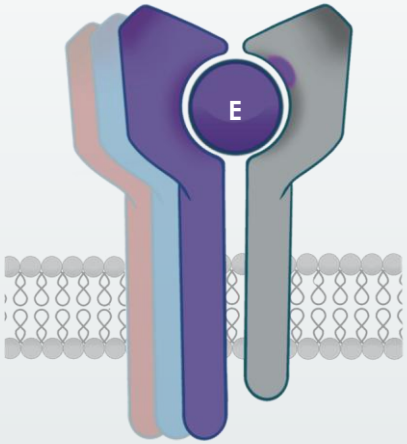
MCi MoA: Disrupting Assembly of the Receptor Complex



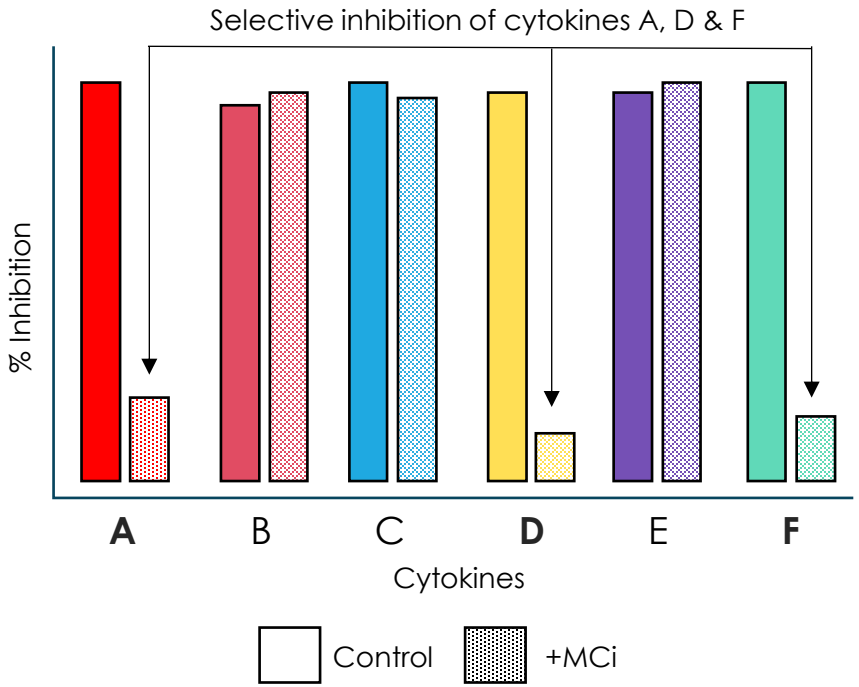
Cytokines first bind to private receptor with high affinity, then transiently dimerize with the γc shared receptor at lower affinity that leads to signaling



No Signaling



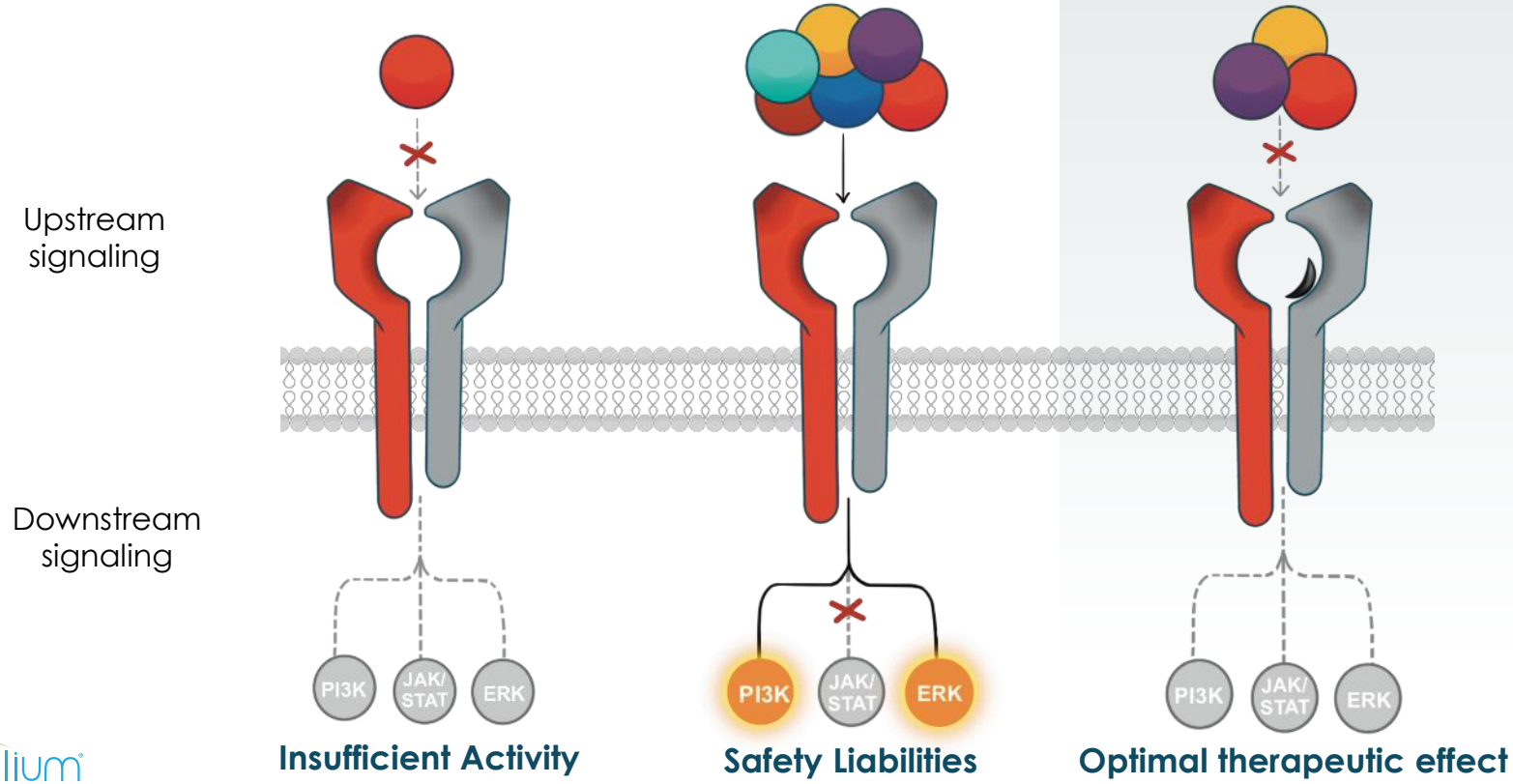
Signaling



Multi-cytokine inhibitor binds to γc receptor and selectively blocks signaling of only selected cytokines e.g., A, D & F

The Multi-Cytokine Inhibitor Advantage

Addressing limitations of single-target biologics and broadly immunosuppressive kinase inhibitors by selectively inhibiting only those cytokines driving disease



Improved Therapeutic Profile

- ✓ Targets undruggable sites not possible with mAb or small molecules
- ✓ Optimized targeting – not too narrow / not too broad
- ✓ Increased selectivity over JAKi can afford improved safety profile
- ✓ Greater potency by inhibiting downstream signaling of targeted cytokines
- ✓ Can be orally or systemically delivered

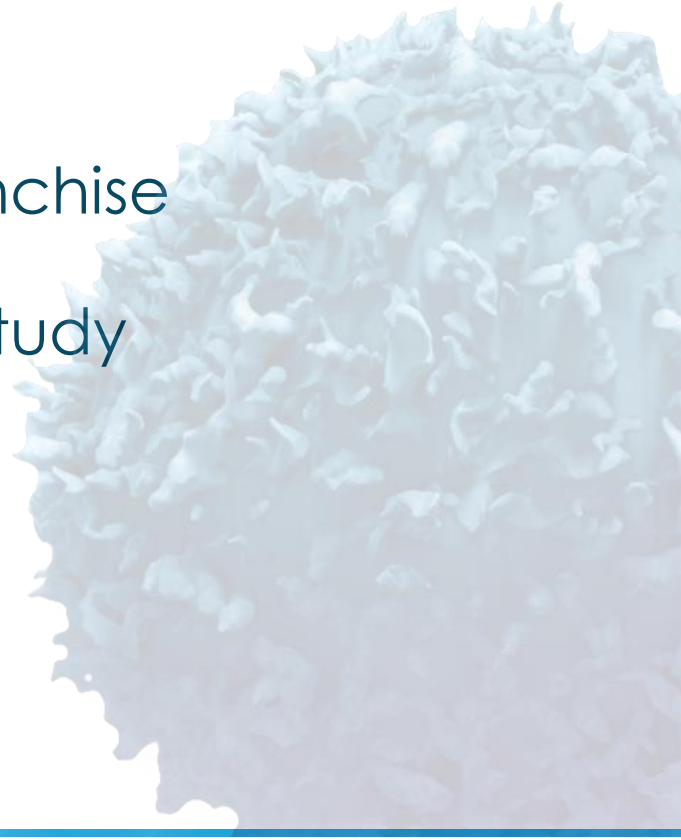
EQ101

First-in-Class Tri-specific inhibitor of IL-2/IL-9/IL-15

Dashboard & Derm Franchise

Alopecia Areata (AA) Study

Phase 2 AA Data



EQ101: First-in-Class Tri-Specific Cytokine Inhibitor

Inhibition of the key cytokines IL-2, IL-9 and IL-15 by EQ101 has shown an **ability to translate from preclinical models into humans**

- IL-2 & IL-15 are important to CD8 and NK cell biology, IL-9 **contributes to inflammation in the skin**[1,2]
- Important to inhibit both IL-2 and IL-15 due to **redundancy in signaling on cytotoxic CD8 T cells**

- PEGylated peptide (based on the D-helix) selectively inhibiting IL-2, IL-9 & IL-15 signaling[3]
- Administered as a low volume intravenous push, with a sub-cutaneous formulation in development

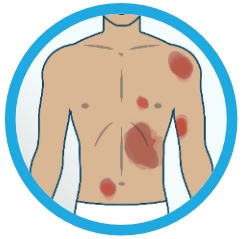
- As active as ruxolitinib in inhibiting multiple lymphoproliferative or leukemic T-cell lines[4,5]
- **More effective than ruxolitinib in mouse model** of immune-mediated hair loss / alopecia areata[6]

- Significant clinical **experience in >135 subjects**, demonstrated favorable safety profile and tolerability[7,8,9]
- **Positive proof-of-concept achieved** in cutaneous T cell lymphoma patients[6]

1) Leonard et al., Immunity Review, 2019 2) Clark et al., Seminars in Immunopathology, 2017 3) Nata et al., J. Biol. Chem., 2015 4) Massoud et al., PNAS, 2015 5) Wang et al., Leukemia, 2018 6) Azimi et al., AHRS, Orlando, Florida, 2018 7) Frohna et al., J. Clin. Pharm., 2019 8) Querfeld et al., Blood, 2019 9) Equillium Inc., Phase 2 alopecia areata study

EQ101: Valuable Medical Dermatology Franchise

Multi-Billion dollar market opportunity for EQ101 in medical dermatology
Large need exists for safe and effective therapies



24,000 adult US Patients[1]

Cutaneous T cell Lymphoma

PoC Achieved & Phase 2/3 Ready - Open IND

- Well tolerated with high ORR in refractory disease
- 2 mg/kg cohort expanded based on early PK/PD & safety, tolerability and efficacy profile

250,000 US moderate-severe Patients[2]

Alopecia Areata

Phase 2 Study complete

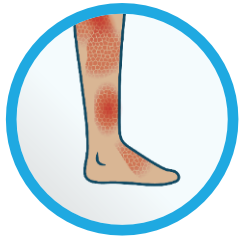
- Only two FDA approvals: JAKi
- Late-stage Industry pipeline is predominantly JAKi
- 2 mg/kg dose used in proof-of-concept based on CTCL study
- Next study expected to include dose optimization

1.5M+ US Patients[3]

Vitiligo

Future Opportunity

- Only one FDA approval: JAKi
- Late-stage Industry pipeline is predominantly JAKi



6.6M US moderate-severe Patients[4]

Atopic Dermatitis

Future Opportunity

- 3 FDA approvals: JAKi
- Large refractory population in need of safer treatment alternatives

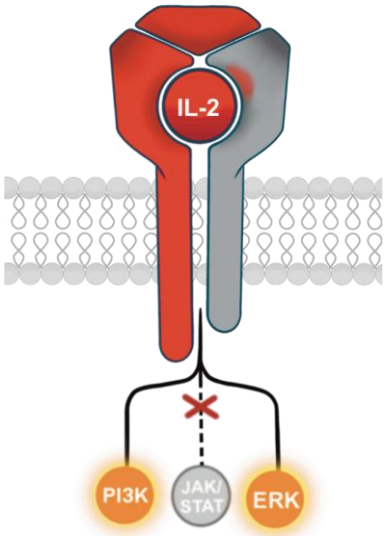
Abbreviation: JAKi, Janus kinase inhibitor

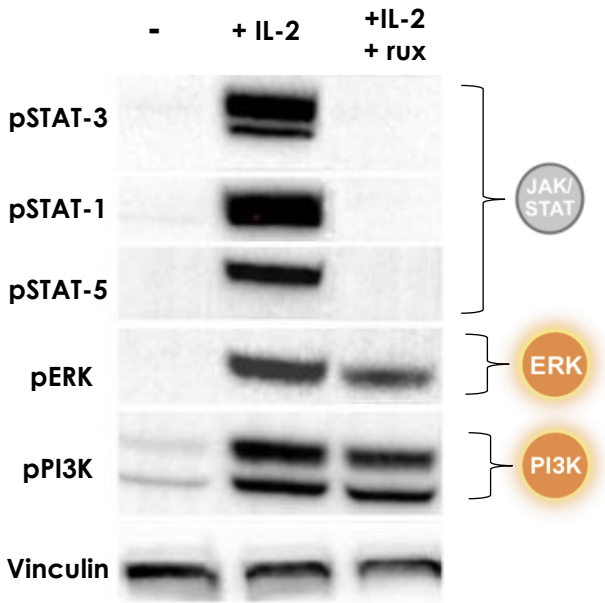
1) Kx Advisors 2) Benigno, Clin Cosmet Investig Dermatol, 2020 3) Bergqvist C, Ezzedine K. Vitiligo: A Review. Dermatology. 2020
4) Chiesa Fuxench ZC, J Invest Dermatol. 2019

EQ101: More Complete Downstream Signal Inhibition Versus JAKi

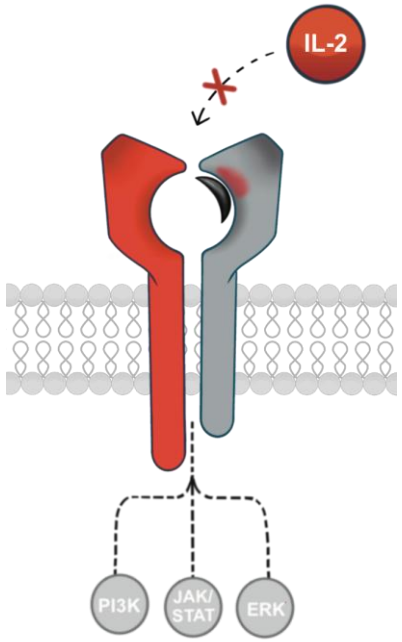
JAKi suppression of cytokine signaling is incomplete, while **EQ101 inhibits the multiple downstream pathways for complete suppression of cytokine signaling**

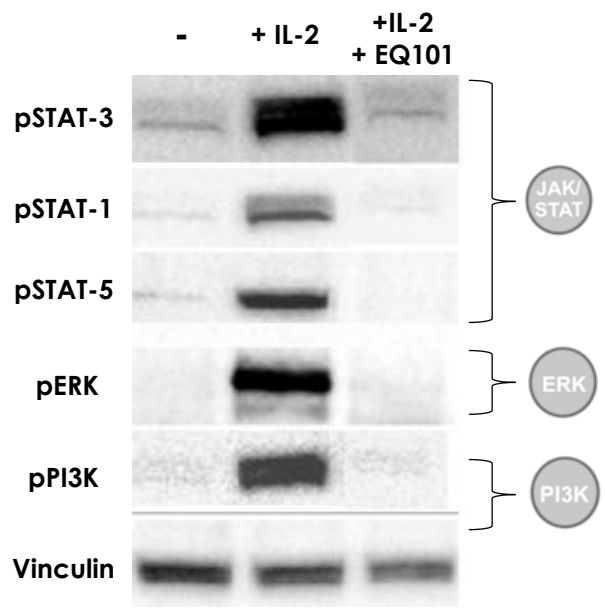
Ruxolitinib blocks JAK/STAT pathway only





EQ101 blocks all major pathways





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

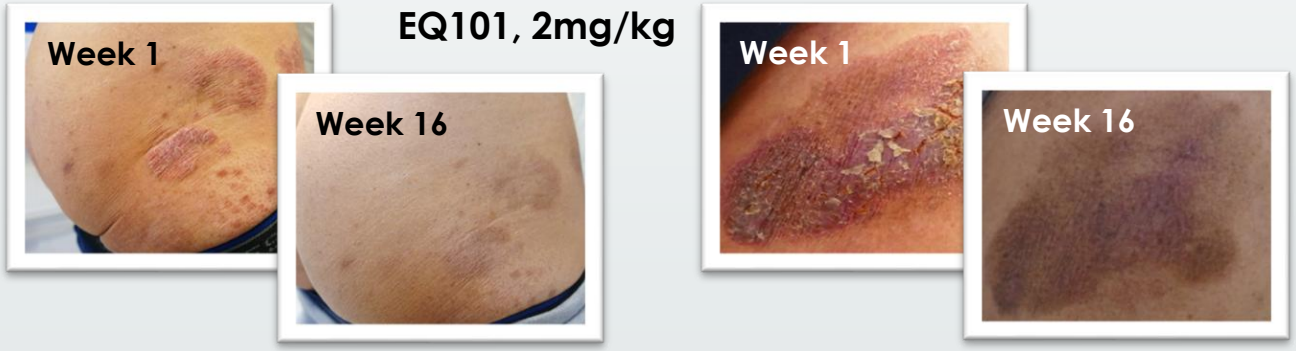
EQ101: Clinically Validated in Severe Dermatological Disease

Favorable safety and tolerability demonstrated in 93 subjects across populations with **compelling clinical activity observed in CTCL patients**

Phase 1/2 MAD study in Cutaneous T Cell Lymphoma (n=30)

- Heavily pre-treated, refractory patient population (median of 5 prior systemic treatments)
- Dose escalation (0.5, 1, 2, 4mg/kg) with 4-week treatment/assessment period (n=30) followed by 12+ week extension (n=19)
- No drug related SAEs, no DLTs and no clinically significant laboratory abnormalities
- Dose-dependent PK/PD correlated with improved skin scores (mSWAT)
- 2mg/kg was selected dose for study expansion and extension

Response Rate in Stage IB/II Patients	
MAVORIC Phase 3 Trial[1]	**EQ101 Phase 1/2**[2]
Mogamulizumab (n=68)	**EQ101 (n=19)**
27.9%	**42.1%**[2]



1) Kim et al., Lancet Oncol., 2018.
2) Querfeld et al., Blood, 2019.
mSWAT = modified severity-weighted assessment
CTCL = Cutaneous T cell Lymphoma

EQ101: Positive Proof-of-Concept Opens Up Indication Expansion

>100 subjects dosed, demonstrated **favorable safety and tolerability**

Compelling clinical activity observed in cutaneous T cell lymphoma (CTCL) patients

Attractive target product profile for the treatment of CTCL patients

IND open and **Phase 3 ready** in CTCL

Use of JAKi in medical dermatology opens up **opportunity for indication expansion**

Now in ongoing **proof-of-concept study in alopecia areata**

Large Unmet Need in Alopecia Areata

EQ101 is positioned as a well-tolerated and effective alternative to JAK inhibitors

Currently approved and late-stage pipeline drugs are all JAK inhibitors

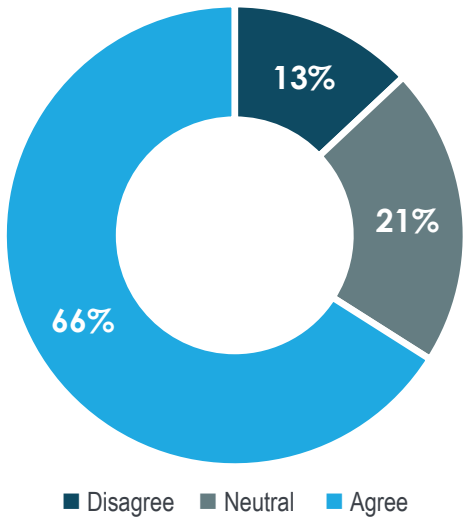
There remains a chronic need, without a safe chronic treatment

Dermatologists indicate safety concerns are the primary barriers to JAKi use in AA patients

79% of physicians surveyed, believe there is an extremely high unmet medical need*

"I am concerned about the safety of oral JAK inhibitors for my AA patients"*

% of respondents, n = 101



Blackbox warning **

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), and THROMBOSIS

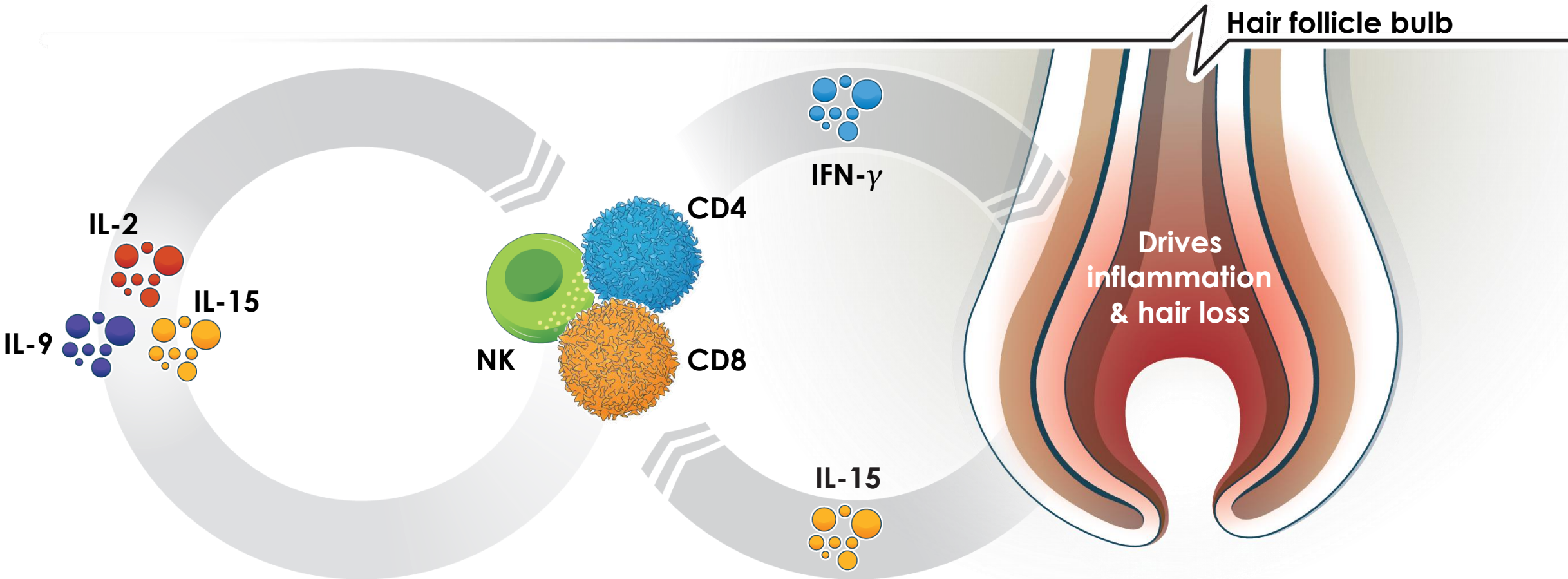
See full prescribing information for complete boxed warning.

- **Increased risk of serious bacterial, fungal, viral and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with OLUMIANT if serious infection occurs until the infection is controlled. OLUMIANT should not be given to patients with active tuberculosis. Test for latent TB before and during therapy, except for COVID-19; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test. (5.1)**
- **Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus kinase inhibitor (JAK) vs. TNF blockers in rheumatoid arthritis (RA) patients. (5.2)**
- **Malignancies have occurred in patients treated with OLUMIANT. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients. (5.3)**
- **Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients. (5.4)**
- **Thrombosis has occurred in patients treated with OLUMIANT. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers. (5.5)**

** Spherix Global Insights, 2022; ** Olumiant Package Insert*

EQ101: Targeted Treatment Approach for Alopecia Areata

IL-2, IL-9 and IL-15 are key drivers of disease in alopecia areata, promoting a cycle of increased IFN-γ production and immune cell attack of the hair follicle



Xing et al., Nat. Med., 2014; Bertolini et al., PLOS, 2014; Suarez-Farinas et al., J Allergy Clin Immunol, 2015; Dai et al., JCI Insight, 2021

EQ101 Reverses Immune-Mediated Hair Loss in a Mouse Model

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

EQ101 Improves Hair Regrowth

EQ101
2 mg/kg
IV 2x/week

Day 0

Day 14

Day 21

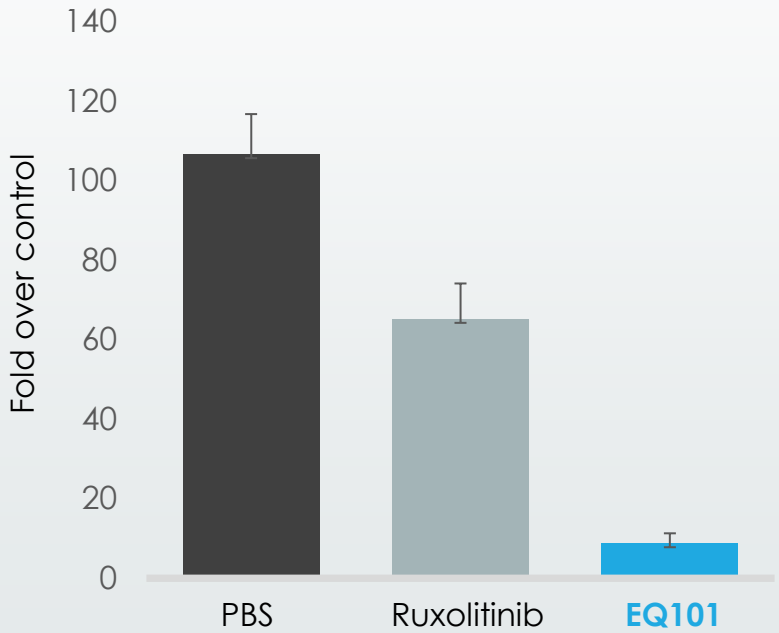
Ruxolitinib
30 mg/kg
2x/day

Day 0

Day 14

Day 21

EQ101 Reduces CD8+ Cytotoxic T-cell Activation Marker NKG2D

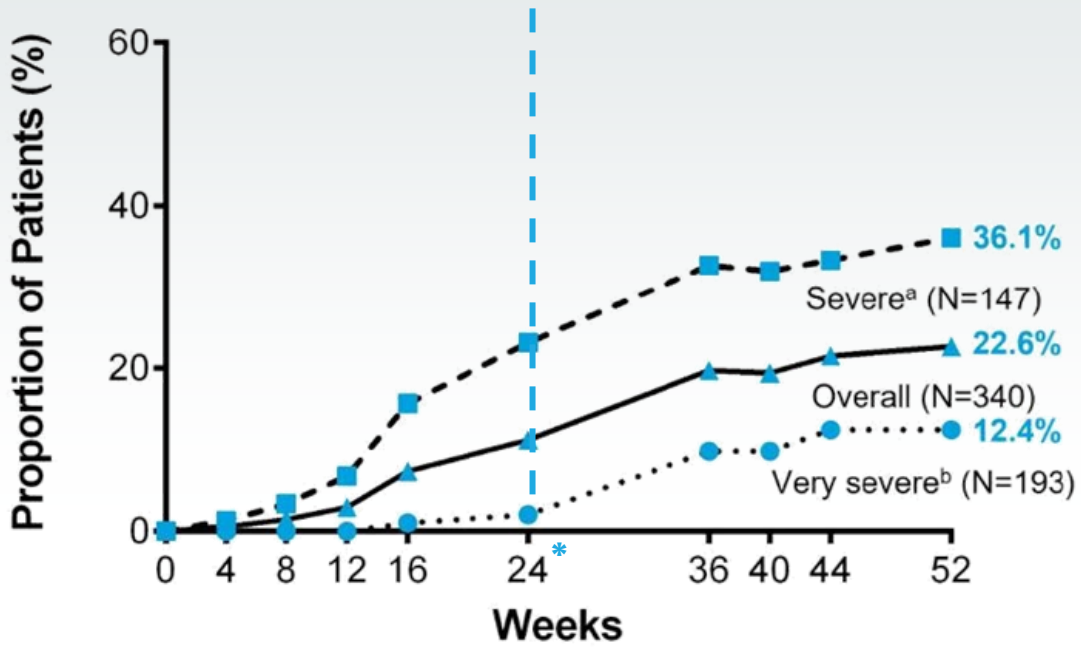


In-house data and Azimi et al., *AHRS*, Orlando, Florida 2018; Frohna, et al., *Alopecia Areata Research Summit*, New York, New York, 2018

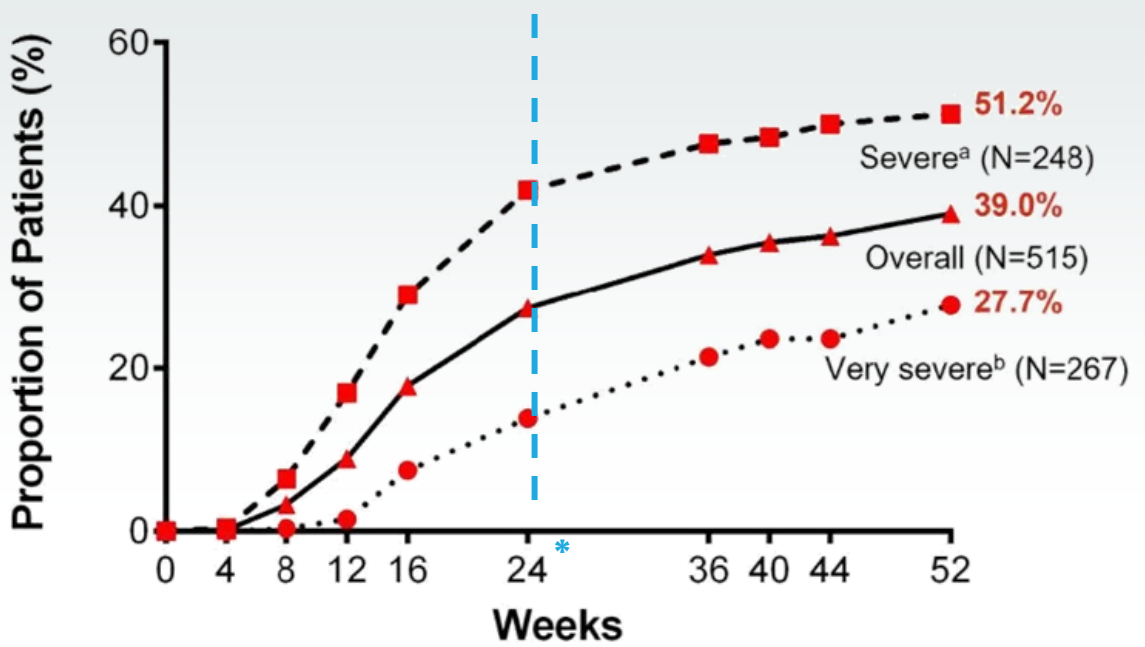
SALT Response Varies by Baseline Severity & Dose

Patients with very severe disease have been shown to be slower to respond and need increased dosing and longer treatment

Baricitinib 2-mg
SALT Score ≤20 Response Rate



Baricitinib 4-mg
SALT Score ≤20 Response Rate



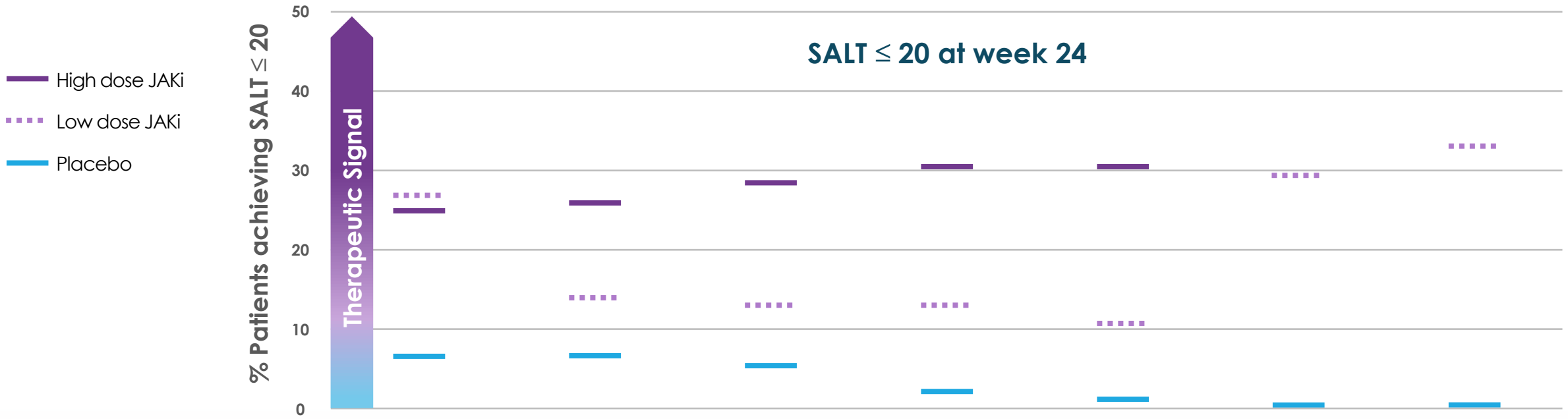
Severe[a]: baseline SALT score of 50-94;
Very severe[b]: baseline SALT Score ≥95

equillium

** EQ101 treatment duration of 24 weeks*
Abbreviation: SALT, severity of alopecia tool; Taylor et al. 2023 Dermatologic Therapy, 13:3181–3191

Comparative Data: SALT ≤ 20 at 24 Weeks

Consistently low placebo rates observed: average of 3.6%
Dose-dependent drug activity observed: range of 11% - 33% in Phase 2 & 3 studies



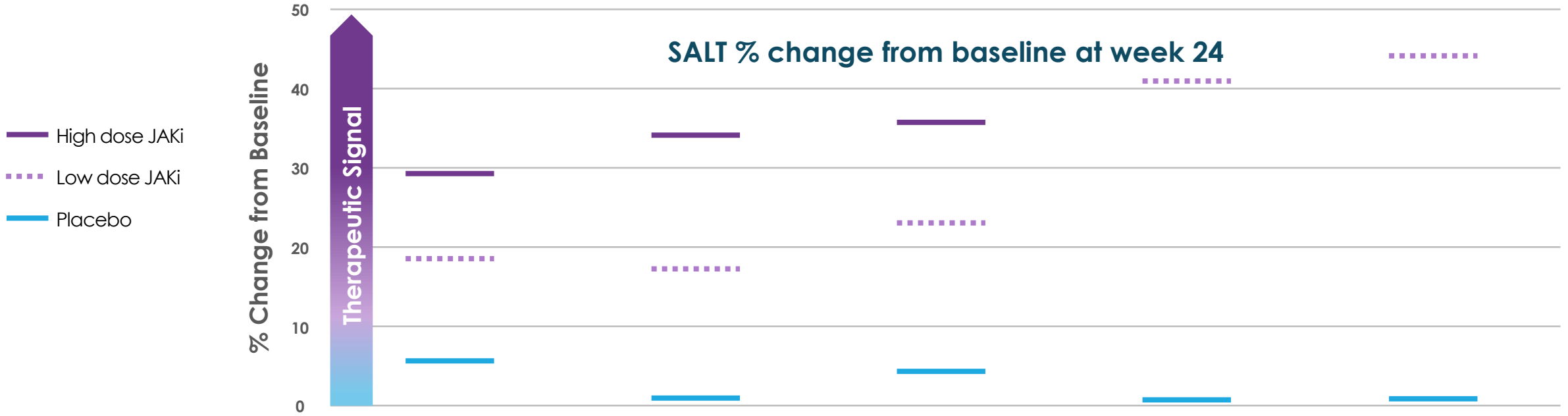
Study	baricitinib BRAVE-AA1 Phase 2[1]	deuruxolitinib Phase 2[2]	baricitinib BRAVE-AA1	baricitinib BRAVE-AA2	ritlecitinib Phase 2/3[3]	deuruxolitinib THRIVE-AA1[4]	deuruxolitinib THRIVE-AA2[2,4]
Baseline SALT: **Active**	86	88	86	85	90	85	88
Baseline SALT: **Placebo**	90		85	85	93	88	

1) Extrapolated 24 wk data, 2) Baseline SALT score data only available as a study average, 3) Low dose 30mg / high dose 200mg loading and 50mg maintenance, 4) Only 8mg dose data used

King et al. 2022 *N Engl J Med*; King et al. 2023 Lancet; Senna et al. 2023 JAAD, presented at AAD, P41701; Sun Pharma PR 2023, AAD Late Breaking News Session; Clinicaltrials.gov NCT04797650; King et al. 2021 J Am Acad Dermatol 85:847-53; King et al. 2021 J Am Acad Dermatol 85:379-87; King et al. 2022 J Am Acad Dermatol

Comparative Data: SALT Change from Baseline at 24 Weeks

Consistently low placebo rates observed: average of 3.2%
Dose-dependent drug activity observed: range of 17% - 45% in Phase 3 studies

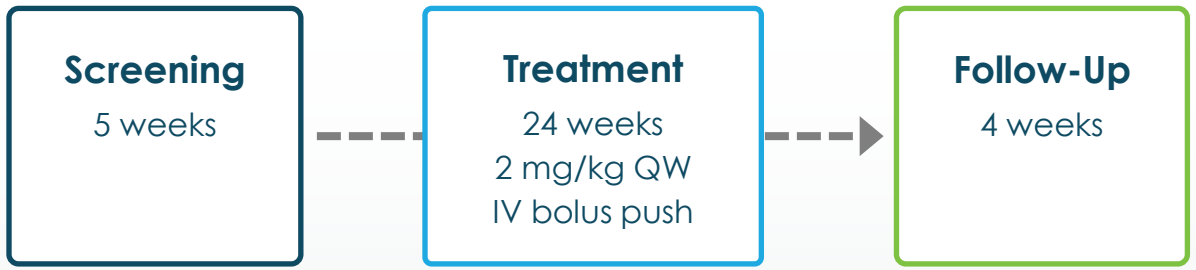


Study	baricitinib BRAVE-AA1	baricitinib BRAVE-AA2	ritlecitinib Phase 2/3[1]	deuruxolitinib THRIVE-AA1[2]	deuruxolitinib THRIVE-AA2[2,3]
Baseline SALT: **Active**	86	85	90	85	88
Baseline SALT: **Placebo**	85	85	93	88	

1) Low dose 30mg / high dose 200mg loading and 50mg maintenance, 2) Only 8mg dose data used, 3) Baseline SALT score data only available as a study average
King et al. 2022 N Engl J Med; King et al. 2023 Lancet; Senna et al. 2023 JAAD, presented at AAD, P41701; Sun Pharma PR 2023, AAD Late Breaking News Session; Clinicaltrials.gov NCT04797650; King et al. 2021 J Am Acad Dermatol 85:847-53; King et al. 2021 J Am Acad Dermatol 85:379-87; King et al. 2022 J Am Acad Dermatol

Phase 2 Study of EQ101 in Adults With Moderate to Very Severe AA

Phase 2 Open Label Study Design



Population N=36

At least 35% scalp hair loss, as defined by a SALT score ≥35

Current episode of hair loss lasting >6 months to <7 years

Study Objectives

Efficacy, Safety & tolerability, PK/PD and biomarkers

Potential Target Product Profile

- Safer alternative to JAKi with comparable efficacy
- Patient-administered weekly/bi-weekly subcutaneous injection (similar to DUPIXENT™)

Abbreviations: AA, alopecia areata; IV, intravenous; JAKi, janus kinase inhibitor; PK/PD, pharmacokinetic/pharmacodynamic; QW, every week; SALT, severity of alopecia tool

Safety Summary: TEAEs

EQ101 exhibited a favorable safety and tolerability profile with no SAEs, similar to the safety profile observed in prior Phase 1 & 2 studies (SAD/MAD NHVs, LGLL and CTCL populations)

SAFETY OVERVIEW

- >70% of subjects had a medical history that included evidence of atopy such as eczema, asthma, or allergies to drugs
- 75% of subjects reported at least 1 TEAE
- There were no Serious TEAEs or Grade 4 or 5 TEAEs
- No notable changes in safety laboratory: coagulation, hematology, chemistry, liver function, urinalysis, cholesterol
- No notable ECG, vital signs, or physical exam findings

Most TEAEs were CTCAE Grade 1 and 2	Only 2 CTCAE Grade 3 TEAEs
73.6% of events were Grade 1 **25.3%** of events were Grade 2 Most common TEAEs (>5 subjects): • Upper respiratory tract infection • Headache • Fatigue	**1.1%** of events were Grade 3 The 2 Grade 3 events in 2 subjects: • Lymphopenia* • Fatigue*

** Subjects discontinued treatment early*

Abbreviations: NHVs, normal healthy volunteers; CTCAE, common terminology criteria for adverse events; CTCL, cutaneous T cell lymphoma; ECG, electrocardiogram; LGLL, large granulocytic lymphocytic leukemia; TEAE, treatment emergent adverse event; SAE, serious adverse event; SAD/MAD, single ascending dose/multiple ascending dose

Key SALT Response Data by Subgroup: Completed Subjects

SALT responses exceed historical placebo rates: greater improvements in moderate and severe subjects (SALT 35 to <95) compared with those with very severe disease (SALT 95+)

SALT Baseline by Subgroups	n (%)	Mean SALT @ Baseline	SALT ≤ 20 @ W24 n (%)	Mean SALT Improvement from Baseline @ W24
35 to <95 (moderate to severe)	**17 (68%)**	**66.1**	**5 (29.4%)**	**18.4%**
35 to <50 (moderate)	*3 (12%)*	*39.9*	*2 (66.7%)*	*23.8%*
50 to <95 (severe)	*14 (56%)*	*71.8*	*3 (21.4%)*	*17.2%*
95 to 100 (very severe, AU/AT)	**8 (32%)**	**99.8**	**0 (0.0%)**	**3.1%**
Completed Subjects **35 to 100**	**25**	**76.9**	**5 (20%)**	**13.5%**

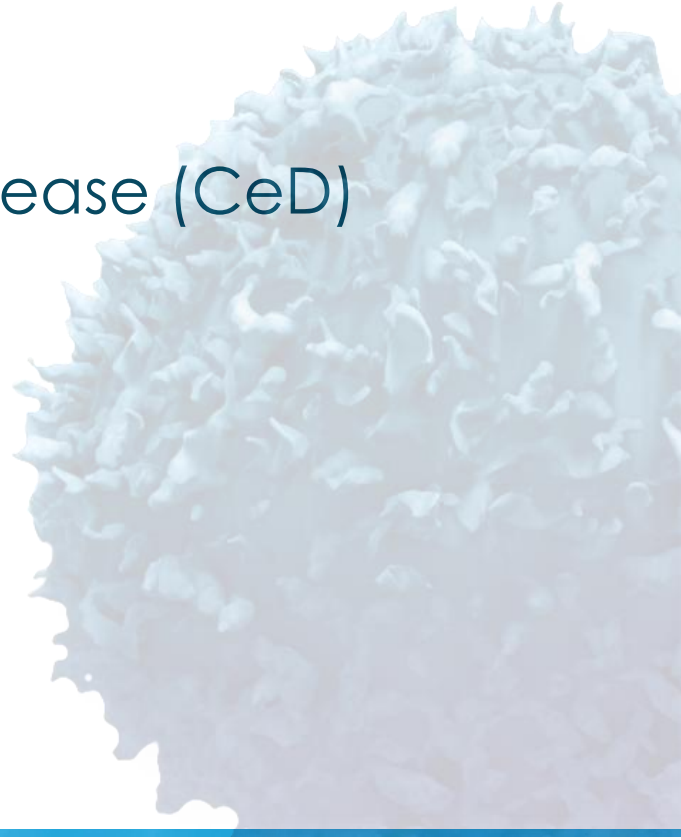
Completed subjects n=25 who completed the 24 weeks of treatment
Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; SALT, severity of alopecia tool; W, week

EQ302

First-in-Class, Orally Delivered
Bi-specific inhibitor of
IL-15 & IL-21

Dashboard & Celiac Disease (CeD)

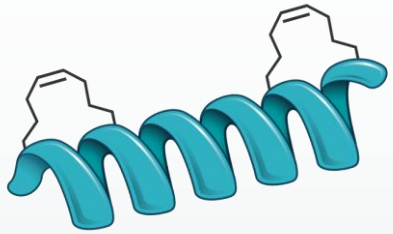
CeD Opportunity



EQ302: First-in-class Bi-Specific Cytokine Inhibitor

IL-15 & IL-21 are **key cytokines driving GI inflammation** in celiac disease and IBD

- IL-15 and IL-21 important to T and B cell biology and **implicated in multiple diseases**
- **Biological synergy of IL-15 and IL-21**
- **IL-15 a validated target** in the treatment of multiple diseases



- **Based on the D-helix of γc cytokines** selectively inhibiting IL-15 & IL-21 signaling
- EQ302 engineered to afford **increased potency, GI stability and permeability**
- Potential for **oral and sub-cutaneous injection**

- **Inhibits the IL-15 & IL-21 induced signaling pathways** in Celiac patient-derived T cells organoid cultures that are key for tissue destruction
- **Prevents intestinal tissue damage** in a humanized mouse model of GI inflammation

- **EQ302 Lead candidate identified**
- **Bioavailable** and therapeutically active target tissue concentrations
- Entering formulation development and **IND-enabling studies**

GI = gastrointestinal; In-house data and Ciszewski et al., Gastroenterology, 2020

EQ302: Valuable Gastrointestinal Franchise

Multi-Billion dollar market opportunity for EQ302 as an **orally delivered bi-specific cytokine inhibitor** for multiple GI indications

2,700,000 adult US Patients[1]

IBD: Crohn's & Colitis

>750,000 US GFD non-responders[2]

Celiac Disease

>350,000 US Patients[3]

Eosinophilic Esophagitis

EQ302 upstream of current cytokine-targeted approaches to treating GI indications


ORIGINAL ARTICLE

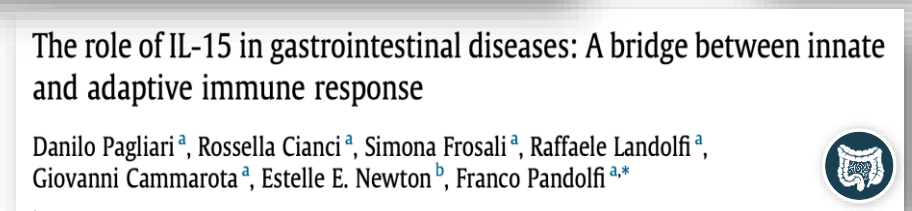
IL-21 Enhances NK Cell Activation and Cytolytic Activity and Induces Th17 Cell Differentiation in Inflammatory Bowel Disease

Zhanju Liu, MD, PhD,* Li Yang, MD, PhD,* Yi Cui, MD,* Xingpeng Wang, MD, PhD,*

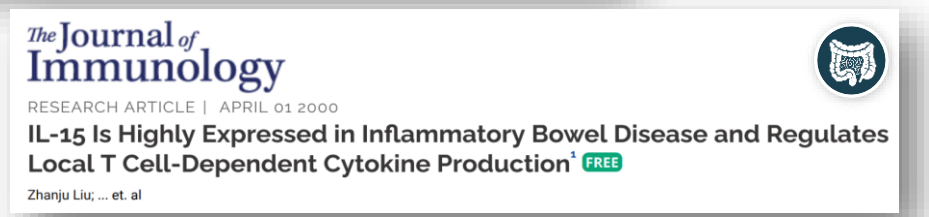

GUIDELINES FOR BASIC SCIENCE

Interleukin-21 triggers effector cell responses in the gut

Daniela De Nitto, Massimiliano Sarra, Francesco Pallone, Giovanni Monteleone


The role of IL-15 in gastrointestinal diseases: A bridge between innate and adaptive immune response

Danilo Pagliari [a], Rossella Cianci [a], Simona Frosali [a], Raffaele Landolfi [a], Giovanni Cammarota [a], Estelle E. Newton [b], Franco Pandolfi [a,*]


The Journal of Immunology

RESEARCH ARTICLE | APRIL 01 2000

IL-15 Is Highly Expressed in Inflammatory Bowel Disease and Regulates Local T Cell-Dependent Cytokine Production[1] FREE

Zhanju Liu; ... et. al

Abbreviations: GFD, Gluten Free Diet

1) gastrojournal.org; 2) Beyond Celiac Website; 3) The American Journal of Gastroenterology 116():p S184-S185, October 2021

No Approved Therapies For Celiac Disease

Celiac Disease:

- Autoimmune disease triggered by consuming gluten resulting in damage to GI tract
- Symptoms include vomiting, diarrhea, abdominal pain, anemia and fatigue
- Many patients non-responsive to strict gluten free diet, experiencing ongoing GI inflammation
- Unresolved inflammation leads to malnutrition, other autoimmune conditions & GI cancers

>750,000

Non-responsive celiac disease patients in the United States

0

Approved Drugs

Multi-Billion Dollar

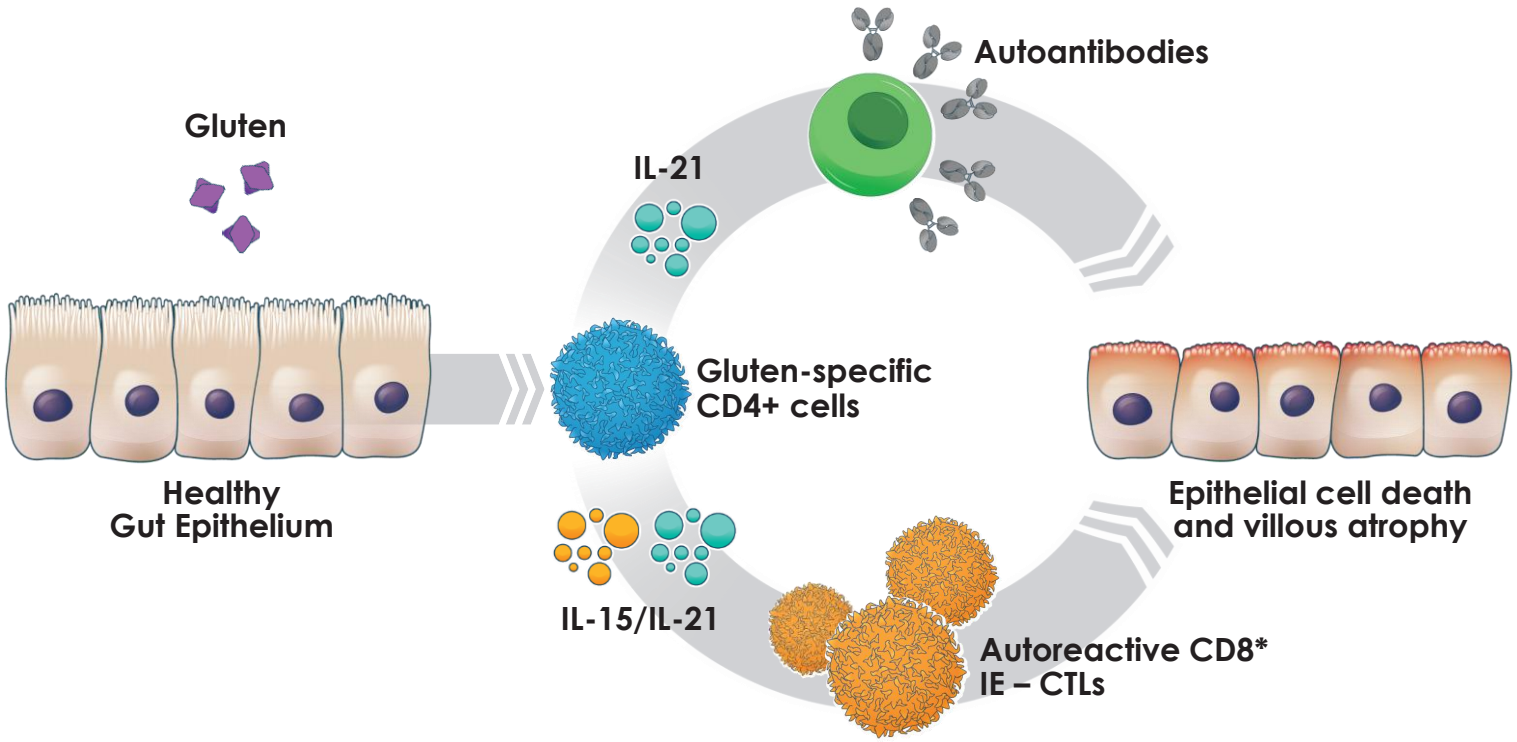
Annual market opportunity

Abbreviations: GI, gastrointestinal

Beyond Celiac Website; Lebwohl et al., Aliment Pharmacol. Ther. 2014 March ; 39(5): 488–495

Celiac Disease: Destructive Immune-mediated GI Disease

IL-15 & IL-21 synergistically drive inflammatory T & B cell responses resulting in tissue damage in celiac patients



Online Submissions: wjg.wjgnet.com
wjg@wjgnet.com
doi:10.3748/wjg.15.4609

World J Gastroenterol 2009 October 7; 15(37): 4609-4614
World Journal of Gastroenterology ISSN 1007-9327
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EDITORIAL

Involvement of interleukin-15 and interleukin-21, two γ-chain-related cytokines, in celiac disease

Daniela De Nitto, Ivan Monteleone, Eleonora Franzè, Francesco Pallone, Giovanni Monteleone

Article

IL-15, gluten and HLA-DQ8 drive tissue destruction in coeliac disease

https://doi.org/10.1038/s41586-020-2003-8
Received: 30 October 2018
Accepted: 16 December 2019
Published online: 12 February 2020

Valérie Abadie, Sangman M. Kim, Thomas Lejeune, Brad A. Palanski, Jordan D. Ernest, Olivier Tastet, Jordan Voisine, Valentina Discepolo, Eric V. Marietta, Mohamed B. F. Hawash, Cezary Ciszewski, Romain Bouziat, Kaushik Panigrahi, Irina Horwath, Matthew A. Zurenski, Ian Lawrence, Anne Dumaine, Vania Yotova, Jean-Christophe Grenier, Joseph A. Murray, Chaitan Khosla, Luis B. Barreiro & Bana Jabri

AUTOIMMUNITY
https://doi.org/10.1080/08916934.2020.1736047

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Serum IL-21 levels from celiac disease patients correlates with anti-tTG IgA autoantibodies and mucosal damage

Erika Iervasi[a,b], Renata Auricchio[c,d], Antonella Strangio[a], Luigi Greco[c,d] and Daniele Saverino[a,b]

[a]Department of Experimental Medicine, University of Genova, Genova, Italy; [b]Laboratory of Autoimmunology, Ospedale Policlinico San Martino, Largo Rosanna Benzi, Genova, Italy; [c]Department of Translational Medical Science, University of Naples Federico II, Napoli, Italy; [d]European Laboratory for Food-Induced disease (ELFID), University of Naples Federico II, Napoli, Italy

ARTICLES

nature publishing group

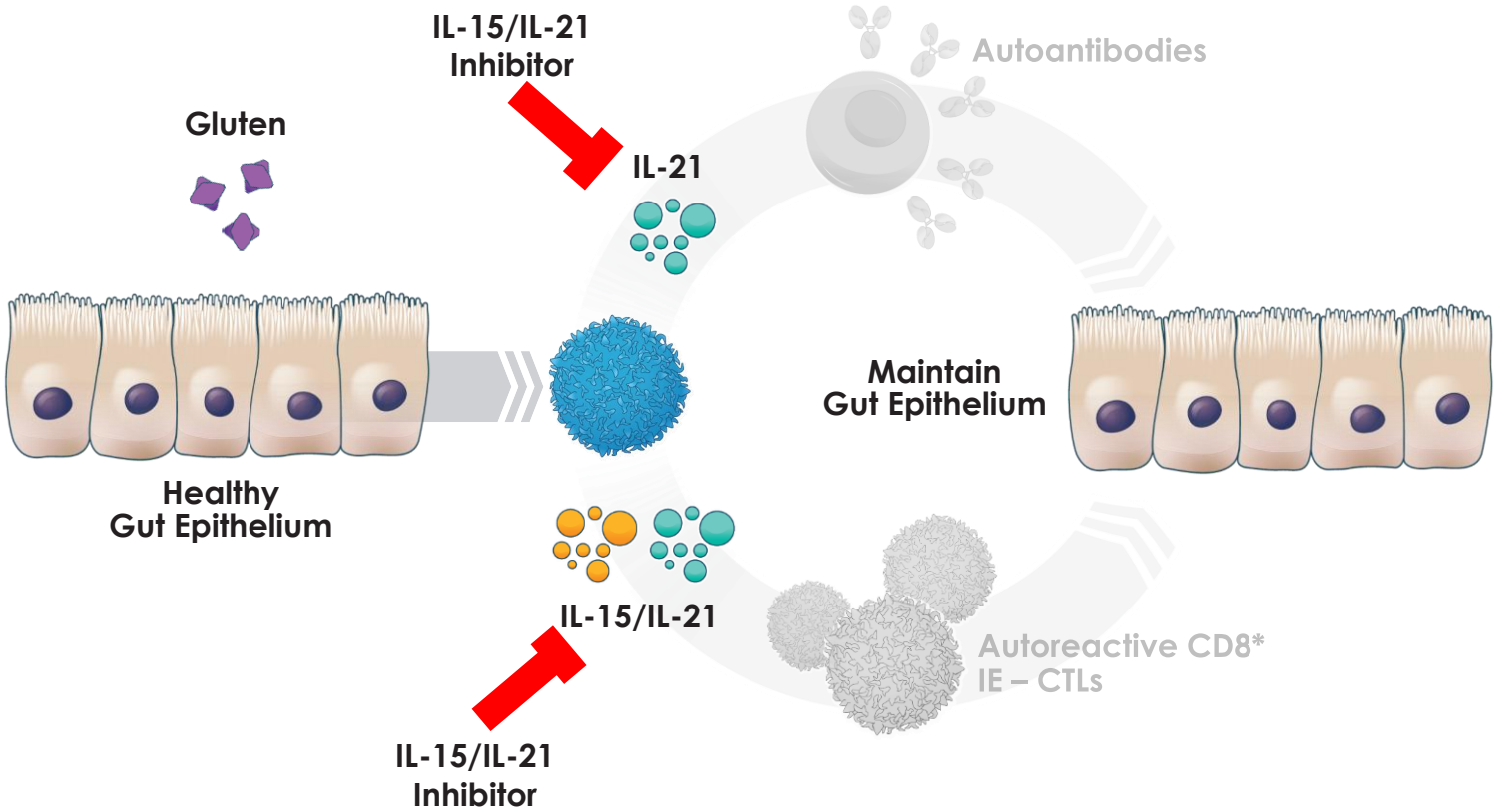
IL-15 positively regulates IL-21 production in celiac disease mucosa

M Sarra[1], ML Cupi[1], I Monteleone[1], E Franzè[1], G Ronchetti[1], A Di Sabatino[2], P Gentileschi[3], L Franceschilli[3], P Sileri[3], G Sica[3], G Del Vecchio Blanco[1], M Cretella[1], OA Paoluzi[1], GR Corazza[2], F Pallone[1] and G Monteleone[1]

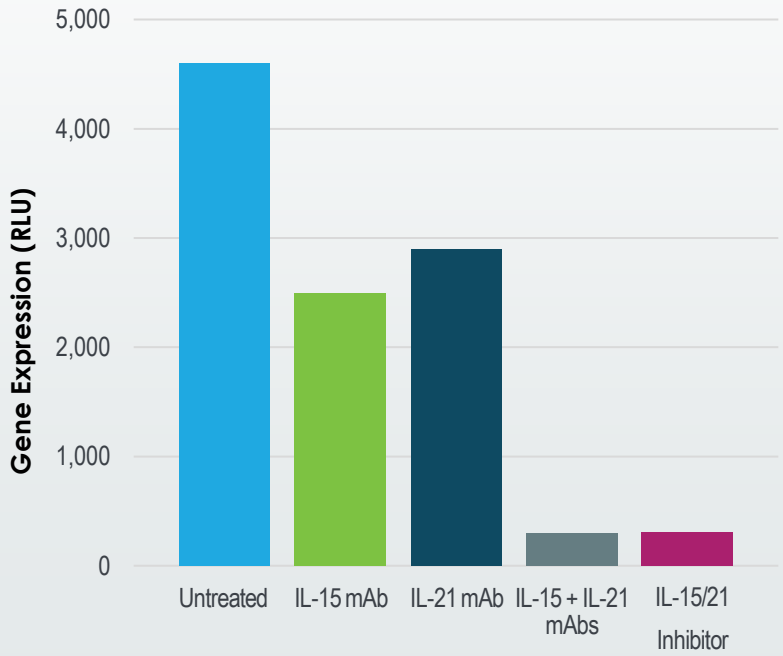
Ciszewski et al., Gastroenterology, 2020
Abbreviations: CeD, celiac disease; IE-CTL, intraepithelial cytotoxic T lymphocyte

A Targeted Treatment Approach for Celiac Disease

Dual inhibition of pathogenic IL-15 & IL-21 pathways that cause inflammation and tissue damage can maintain healthy gut epithelium



Inhibition of Granzyme B expression in CeD IE-CTLs stimulated with IL-15 & IL-21

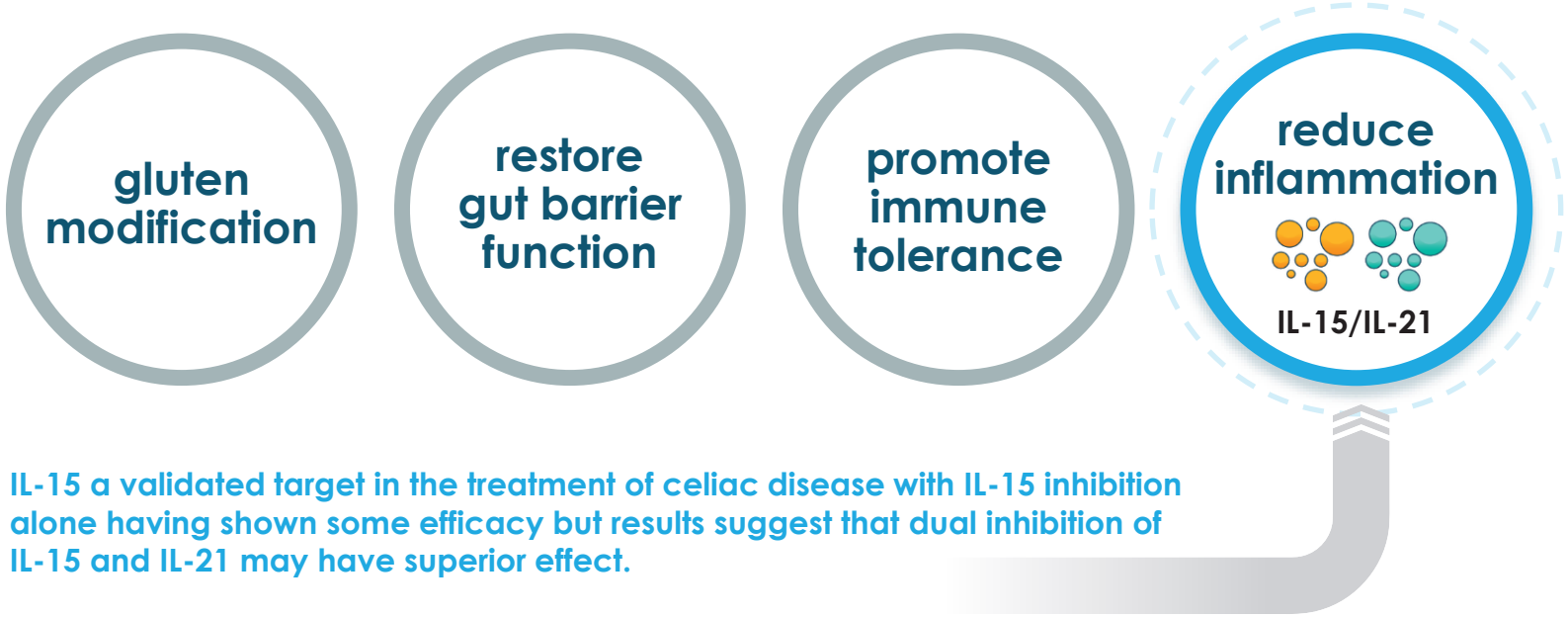


Ciszewski et al., Gastroenterology, 2020; Frohna et al., 17th International Celiac Disease Symposium, New Delhi, 2017
Abbreviations: CeD, celiac disease; IE-CTL, intraepithelial cytotoxic T lymphocyte

Opportunity in Celiac Disease

EQ302 selectively targets the underlying immune pathophysiology, and the targeted approach **aligns with FDA guidance to treat inflammation**

Approaches to Treating Celiac Disease



IL-15 a validated target in the treatment of celiac disease with IL-15 inhibition alone having shown some efficacy but results suggest that dual inhibition of IL-15 and IL-21 may have superior effect.

Increasing Regulatory Clarity and Strategic Interest in Celiac Disease

AMGEN · Pfizer · NOVARTIS · Takeda

FDA guidance* was recently updated and provides clear guidelines for path to approval. Emphasis has been placed on development of effective anti-inflammatory strategies.

* *https://www.fda.gov/media/157682/download*