

Introduction to Priovant

November 2022

**priovant**
therapeutics

Anchor Asset: Brepocitinib Potential First-In-Class Dual Inhibitor of TYK2 and JAK1

Brepocitinib Highlights

Novel Mechanism: Dual inhibition of TYK2 and JAK1 is expected to provide greater efficacy than agents that inhibit either alone in multiple highly inflammatory autoimmune diseases

Robust Clinical Data: Statistically significant and clinically meaningful benefit in all five placebo-controlled studies completed to-date in oral formulation (once-daily administration)

Well-Characterized Safety Profile: Exposure in >1,000 subjects and patients suggests safety profile consistent with approved JAK inhibitors

Distinctive Strategy: Rather than standard set of highly competitive JAK inhibitor indications, pursue series of orphan and specialty autoimmune diseases with few approved therapies, high morbidity and mortality, and pathobiologies for which we expect that both TYK2 and JAK1 inhibition will contribute to efficacy

Two Ongoing Registrational Programs: Single registrational phase 3 study in dermatomyositis (DM) initiated Q2 2022; large, global phase 2B study in systemic lupus erythematosus (SLE), designed to serve as one of two registrational studies, is fully enrolled (data anticipated in 2H 2023)

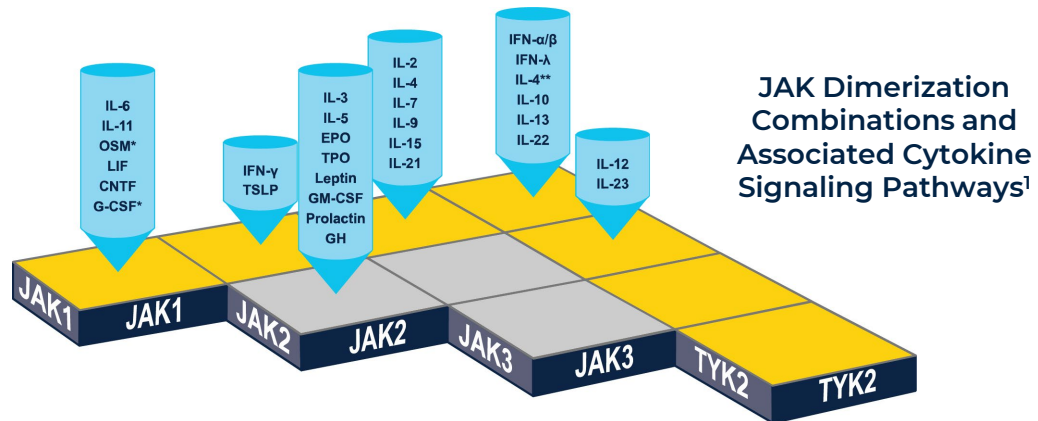
ORAL BREPOCITINIB

Potential First-In-Class Dual Inhibitor of TYK2 and JAK1

Dual TYK2/JAK1 Inhibition: distinctive benefits for suppression of key cytokines linked to autoimmunity

Optimized for suppression of type I IFN signaling

Ability to suppress each of IFN α/β , IFN γ , IL-6, IL-12, and IL-23 through a single agent



Breprocitinib is the only dual inhibitor of TYK2 and JAK1 in late-stage development; none are approved

Molecule	Isoform Selectivity	Latest Development Phase
Breprocitinib	TYK2/JAK1	Phase 3
XELJANZ (tofacitinib)	JAK1/JAK3	Approved
JAKAFI/OPZELURA (ruxolitinib)	JAK1/JAK2	Approved
OLUMIANT (baricitinib)	JAK1/JAK2	Approved
RINVOQ (upadacitinib)	JAK1	Approved
CIBINQO (abrocitinib)	JAK1	Approved
SOTYKTU (deucravacitinib)	TYK2 ²	Approved
Ritlecitinib	JAK3/TEC	NDA submitted

1) Adapted from Murray et al, 2007 and Morris et al, 2018
2) Allosteric

* JAK1 is dominant, but these receptors also bind JAK2 and TYK2
** Type II

ORAL BREPOCITINIB

Statistically Significant and Clinically Meaningful Results Across Five Completed Phase 2 Studies

Study Population	N ¹	Brepocitinib Dose	Primary Endpoint Result	Statistical Significance
Psoriatic Arthritis Patients with active PsA	218	30 mg once daily	23.4% placebo-adjusted ACR20 RR at week 16	P = 0.0197
Plaque Psoriasis Patients with moderate-to-severe PsO	212	30 mg once daily	-10.1 placebo-adjusted CFB in PASI Score at week 12	P < 0.0001
Ulcerative Colitis Patients with moderate-to-severe UC	167	30 mg once daily	-2.28 placebo-adjusted CFB in Mayo Score at week 8	P = 0.0005
Alopecia Areata Patients with moderate-to-severe AA	94 ²	30 mg once daily ³	49.18 placebo-adjusted CFB in SALT Score at week 24	P < 0.0001⁴
Hidradenitis Suppurativa Patients with moderate-to-severe HS	100	45 mg once daily ⁵	18.7% placebo-adjusted HiSCR Rate at week 16	P = 0.0298⁴

CONSISTENT, REPRODUCIBLE CLINICAL BENEFIT OBSERVED ACROSS WIDE RANGE OF AUTOIMMUNE INDICATIONS

1) Overall study N represents patients randomized to all brepocitinib dose levels or placebo and excludes patients randomized to other agents

2) Includes patients from initial 24-week study period only

3) 60 mg QD for 4 weeks followed by 30 mg QD for 20 weeks

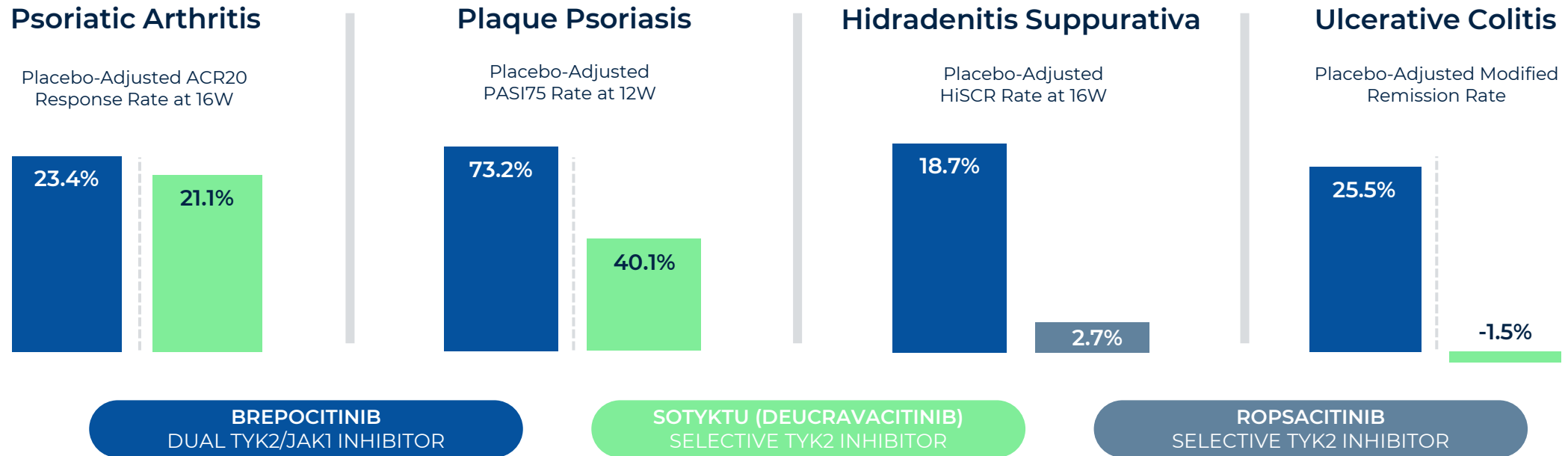
4) One-sided p-value (pre-specified statistical analysis)

5) Brepocitinib 45 mg once daily was the only brepocitinib dose evaluated in this study

CFB: change from baseline; RR: response rate

Clinical Experience Supports Value Of Dual TYK2/JAK1 Inhibition As Compared To Selective TYK2 Inhibition

In all indications where oral brepocitinib and a selective TYK2 inhibitor have been evaluated, brepocitinib's observed efficacy has been numerically greater



Psoriatic arthritis, plaque psoriasis, and ulcerative colitis: no direct head-to-head data available – cross-trial comparison of studies with different inclusion-exclusion criteria and design elements

Psoriatic Arthritis: brepocitinib 30 mg QD (Phase 2B – 16W; Data on file) vs. deucravacitinib 6 mg QD (Phase 2 – 16W, NCT03881059; Mease et al, Ann Rheum Dis 2022)

Plaque Psoriasis: brepocitinib 30 mg QD (Phase 2 – 12W; Data on file) vs. deucravacitinib 6 mg QD (Phase 3 POETYK-PSO-2 – 12W, NCT03611751; Armstrong et al, SDDS 2021 Poster 1042)

Hidradenitis Suppurativa: brepocitinib 45 mg QD vs ropsacitinib 400 mg QD (Phase 2 – 16W, NCT04092452; Data on file)

Ulcerative Colitis: brepocitinib 30 mg QD (Phase 2B – 8W; Data on file) vs. deucravacitinib 6 mg BID (Phase 2 LATTICE-UC – 12W, NCT03934216; Danese et al, ECCO 2022)

Note: where more than one value is available for a competitor molecule (e.g., in the case of two Phase 3 studies), the higher value was selected for comparison to brepocitinib

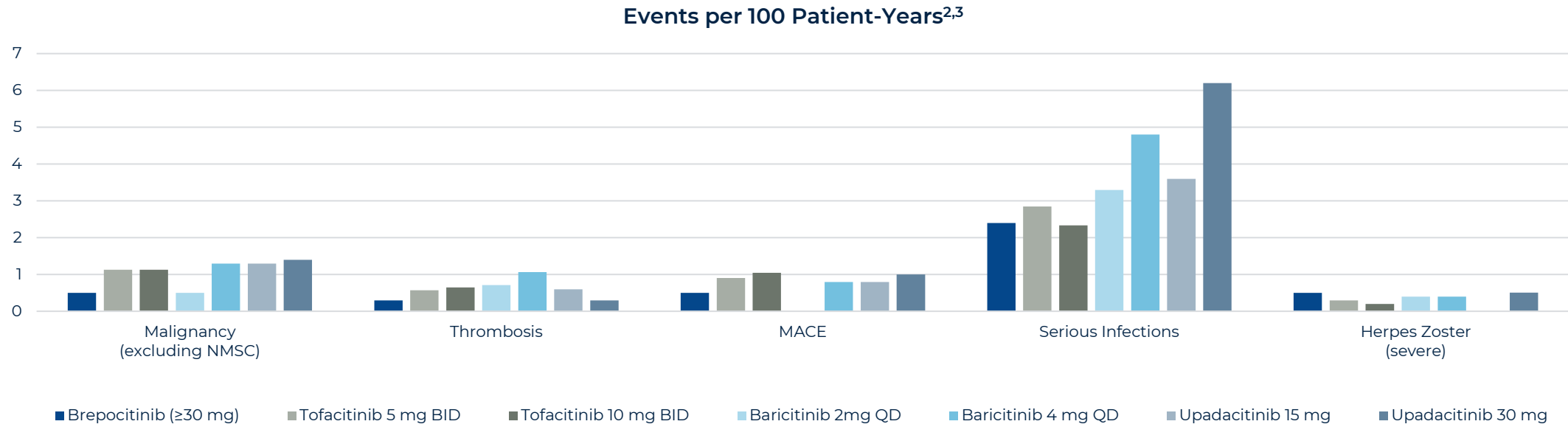
ORAL BREPOCITINIB

Safety Overview

Clinical experience in more than 1,000¹ exposed subjects and patients suggests a safety profile consistent with those of approved JAK inhibitors

Comparable Incidence Rates of TEAEs of Interest vs. Approved JAKs

No direct head-to-head data available – cross-trial comparison of studies with different inclusion-exclusion criteria and design elements



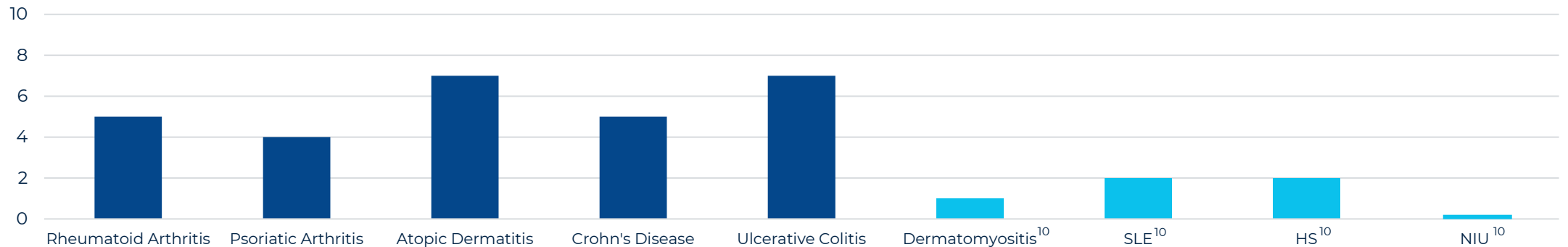
1) Total exposure count includes 8 completed Phase 1 studies and 6 completed Phase 2 studies (PsA, PsO, AA, UC, Vitiligo, and HS) in addition to 2 ongoing Phase 2 studies (SLE and Crohn's).
 2) Analysis includes only completed studies. Some patients received multiple dose levels. For any given dose level, patients are counted only once. Breprocitinib ≥30 mg comprises over 90% of aggregated patient-years of breprocitinib exposure in this analysis. Note that all data are shown as Events per 100-Patient Years except for tofacitinib, which is provided as Subjects with Event per 100 Patient-Years.
 3) References for this chart provided in Appendix 1.

PRIOVANT STRATEGY

A New Approach to JAK Inhibitor Development

Indications with highest unmet need, where dual inhibition of TYK2 and JAK1 is expected to provide greater efficacy than inhibiting either alone → opportunity for brepocitinib to become a leading treatment option

JAK Inhibitors Approved or in Development¹



Est. US Prevalence	1,500,000 ²	600,000 ³	>25,000,000 ⁴	800,000 ⁵	900,000 ⁵	37,000 ⁶	300,000 ⁷	170,000 ⁸	75,000 ⁹
Approved Therapies¹¹	>20	14	8	7	12	1	4	1	1

Historical Focus of JAK Development

Higher prevalences, highly competitive commercial landscapes, wide range of symptom severity

Priovant Focus

High morbidity and mortality, with few approved therapies and no approved JAK inhibitors

1) Includes JAK inhibitors in company-sponsored Phase 2 trials or beyond; excludes combination studies
 2) Arthritis Foundation
 3) Karmacharya et al, Arth Rheum (2021)
 4) National Eczema Foundation

5) Crohn's and Colitis Foundation
 6) PriovantTx estimates based on Reeder et al (2010), Smoyer-Tomic et al (2012), and claims analysis (Adult DM only)
 7) Centers for Disease Control
 8) Phan et al, Biomed Derm (2020); includes only moderate/severe patients

9) Thorne et al, JAMA Ophthalmol. (2016)
 10) Excludes brepocitinib
 11) Source: GlobalData; excludes glucocorticoids and corticotropin injection

BREPOCITINIB

Pipeline-in-a-Product

Potential franchise across multiple blockbuster orphan and specialty autoimmune indications

	Key Pathogenic Cytokines	EXPLORATION	PROOF OF CONCEPT	REGISTRATION-ENABLING	
Dermatomyositis (Oral)	IFN α/β , IFN γ , IL-12, IL-23				<ul style="list-style-type: none"> • Single Phase 3 study underway • Potential TLR in 2H 2025
Systemic Lupus Erythematosus (Oral)	IFN α , IFN γ , IL-6, IL-12, IL-23				<ul style="list-style-type: none"> • Phase 2B study ongoing (potentially 1 of 2 registrational studies); study is fully enrolled • TLR anticipated 2H 2023
Hidradenitis Suppurativa (Oral)	IFN γ , IL-12, IL-23				<ul style="list-style-type: none"> • Positive Phase 2 data in 1H 2022
Non-Infectious Uveitis (Oral)	IFN γ , IL-6, IL-12, IL-23				<ul style="list-style-type: none"> • Phase 2 POC study underway
Other Indications (Oral & Topical)	Various TYK2- and JAK1-linked cytokines				<ul style="list-style-type: none"> • POC studies under evaluation

Dermatomyositis





GOTTRON'S PAPULES

Red to violaceous papules overlying the knuckles



V-SIGN RASH

Irregular, patchy erythema on the chest

Dermatomyositis: A Debilitating Inflammatory Myopathy

Dermatomyositis is a rare, chronic, immune-mediated disease of the muscles and skin affecting approximately 37,000¹ adults in the United States

Clinical Presentation

Average Age of Onset	40-60 years²
Proximal muscle weakness	88%³
Characteristic rash	Gottron's papules: 54%³ Heliotrope rash: 74%³ Nailfold changes: 43%⁴
Malignancy	9-32%⁵
Interstitial lung disease	42%⁶
Chronic or refractory disease	63%⁷
Mortality	10-40% at five years⁵

Unmet Need

Only approved therapy (other than glucocorticoids and corticotropin) is IVIg – difficult administration and associated with severe side effects

Thrombotic events are estimated to occur in 1-17% of patients receiving IVIg therapy⁸

~30% of dermatomyositis patients are unable to discontinue long-term steroid-based treatment due to refractory disease⁹

Need for novel, targeted therapies that address underlying DM pathobiology in chronic, refractory patients

1) PriovantTx estimates based on Reeder 2010, Smoyer-Tomic 2012, and claims analysis
 2) National Organization for Rare Diseases
 3) Fardet et al, Medicine (2009)
 4) Selva-O'Callaghan et al, Sem Arth Rheum (2010)

5) Liu et al, Oncol Letters (2018)
 6) Sun et al, Sem Arth Rheum (2021)
 7) Robinson et al, Nat Rev Rheum (2011)
 8) Guo et al, Front Immunol (2018)
 9) Syneos Health Research

Dermatomyositis Prevalence

Increasing disease awareness and diagnosis has led to higher incidence and prevalence estimates over time; Priovent estimates there are approximately 37,000 adult DM patients in the United States

ESTIMATED PREVALENCE PER 100,000

Ahlstrom et al (1993)
County-specific study in Sweden



Smoyer-Tomic et al (2012)
US healthcare claims data analysis from 2004-2008



Reeder et al (2010)
Medical record analysis of residents of Olmsted County, MN from 1976-2007



Priovent Claims Analysis
Analysis of Komodo claims database from 2016-2020



A prevalence rate of **~14/100,000** individuals implies approximately **37,000** adult patients in the United States with dermatomyositis

Rationale for Brepocitinib in Dermatomyositis

1. Clinical evidence from investigator-initiated study of tofacitinib in DM and >100 off-label case reports (Paik et al, 2022)¹ suggest that JAK inhibition may be efficacious in DM
2. DM pathobiology is driven by dysregulations in cytokines whose signaling is mediated by both TYK2 and JAK1 (especially Type I interferon), suggesting potentially greater efficacy for brepocitinib compared to tofacitinib and selective TYK2 or JAK1 inhibitors
3. Cross-study comparisons of brepocitinib 30mg daily to tofacitinib in other autoimmune indications suggests dosing brepocitinib at 30mg daily may generate clinically meaningful efficacy in DM

Given strong clinical and pharmacologic rationale in an orphan indication with high unmet need, Priovent has advanced brepocitinib directly into a single Phase 3 study

1) Paik et al, Clin Exp Rheum 2022 (in press)

JAK INHIBITION IN DERMATOMYOSITIS

Clinical Proof-of-Concept

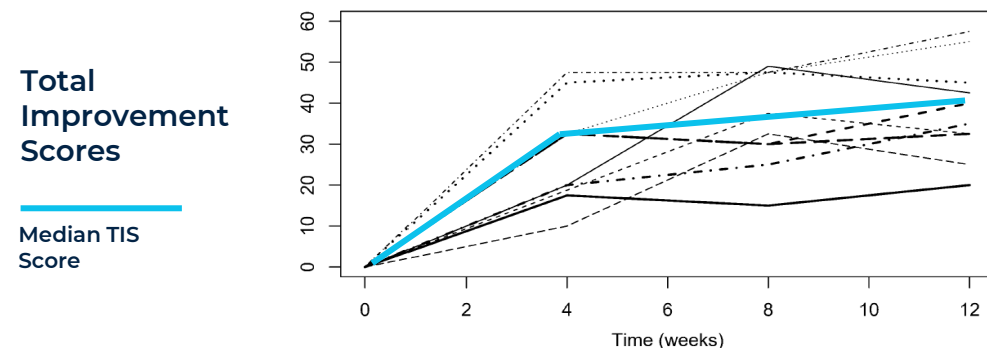
Previous clinical study and case literature support the use of JAK inhibitors in dermatomyositis

Study of Tofacitinib in Refractory Dermatomyositis (STIR)¹

Open-label study evaluating tofacitinib 11 mg XR in adults with refractory dermatomyositis

Primary endpoint: Total Improvement Score, a validated composite endpoint of six measures of disease activity (regulatory approval endpoint)

All ten subjects demonstrated clinically meaningful response (TIS20 Response Rate at Week 12: 100%)



Dermatomyositis Case Reports

Systematic literature review² identified 145 total cases of DM (n=84) and juvenile dermatomyositis (JDM) (n=61) treated with JAK inhibitors

~62% of cases were treated with tofacitinib (JAK1/3); remainder with other JAK inhibitors

Most patients were initiated on JAK inhibitors for refractory disease and had failed SOC treatment

Key Results

Of 145 profiled subjects, 137 were considered clinical successes or responders by their respective investigators, with sustained improvement through most recent follow-up

Objective and subjective improvements noted in muscle disease, skin disease, and in DM-ILD

1) Paik et al, Arth Rheum 2020
2) Paik et al, Clin Exp Rheum 2022

KEY PATHOGENIC CYTOKINE IN DERMATOMYOSITIS

Type I Interferon

There is substantial evidence that dermatomyositis is a type I interferon-driven disease; brepocitinib's dual inhibition of TYK2 and JAK1 may provide best-in-class type I IFN suppression

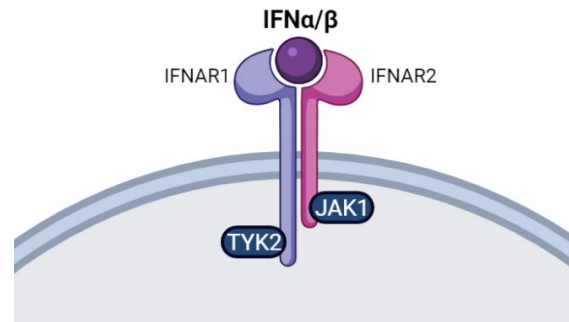
Type I IFN is the key pathogenic cytokine in dermatomyositis

Elevated levels of type I IFN have been found in the skin¹, muscle², and blood³ of patients with dermatomyositis

Type I IFN gene signature scores correlate with DM disease activity, decrease with immunomodulatory therapy, and shift concordantly with major changes in disease activity^{3,4}

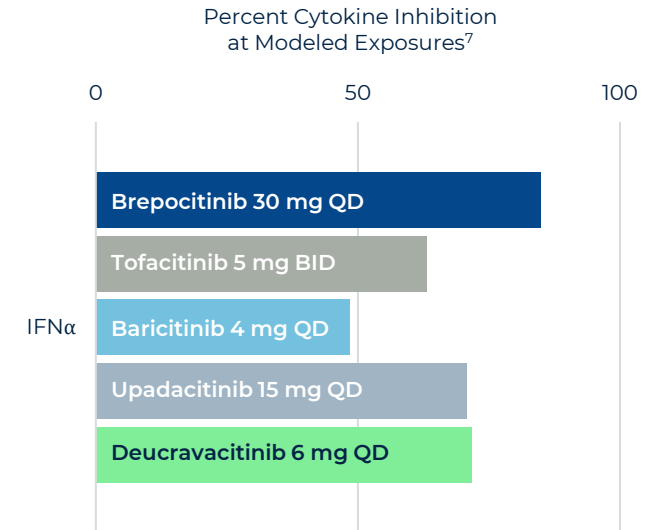
Application of type I IFN to cultured myotubes results in decreased surface area and increased expression of atrophy-associated genes⁵

Type I IFN signal transduction is mediated by the dual activity of TYK2 and JAK1



Identification of catalytically-deficient TYK2 and JAK1 mutants with full IFN signaling competency suggests inhibition of both TYK2 and JAK1 is required for maximal type I IFN suppression⁶

Whole blood assays suggest brepocitinib may provide best-in-class suppression of type I IFN



Cross-study comparisons with different assay conditions

1) Wong et al, 2012
2) Greenberg, Curr Opin Rheum 2010
3) Greenberg et al, Genes Immun 2012

4) Huard et al, Br J Dermatol 2017
5) Ladislau et al, Brain 2018
6) Li et al, J Immunol 2013

7) Calculations based upon whole-blood inhibition assays as reported in Dowty et al (2019) and in the Brepocitinib Investigator's Brochure. See Appendix 1 for further references.

SUPPRESSION OF MULTIPLE PATHWAYS

Other TYK2- and JAK1-Mediated Cytokines

In addition to type I interferon, several other inflammatory cytokines contribute to dermatomyositis pathophysiology and are inhibited by brepocitinib

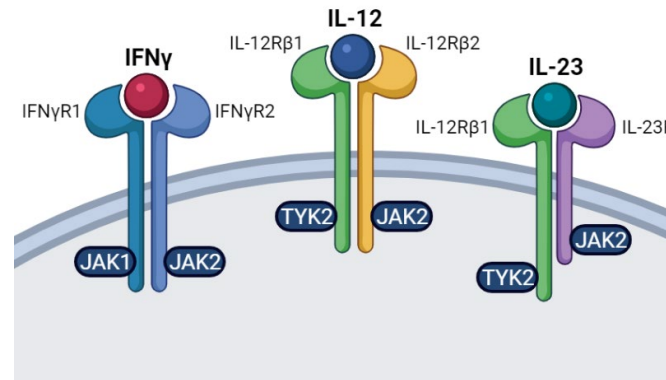
Other key cytokines: IFN γ , IL-12, and IL-23

IFN γ : Upregulated in the muscle¹ and blood² of patients with dermatomyositis; enhances inflammation in the muscle¹ and contributes to macrophage polarization and infiltration in the lungs²

IL-12: Elevated in the serum of patients with pulmonary complications of dermatomyositis (interstitial lung disease)²

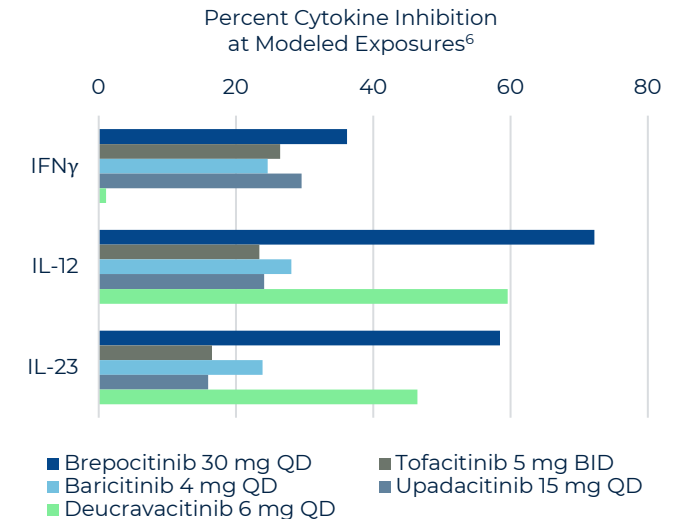
IL-23: Elevated in the blood of patients with dermatomyositis³; produced by macrophages in damaged muscle and contributes to further muscle infiltration/ inflammation via potentiation of antigen presentation and cytokine production^{4,5}

IFN γ , IL-12, and IL-23 signaling is mediated by JAKs inhibited by brepocitinib



Brepocitinib's potent inhibition of TYK2 and JAK1 is expected to result in substantial inhibition of IFN γ , IL-12, and IL-23

Whole blood assays suggest brepocitinib may provide best-in-class suppression of IFN γ , IL-12, and IL-23



Cross-study comparisons with different assay conditions

1) Giris et al, In Vivo 2017
2) Ishikawa et al, Arth Res Ther 2018
3) Shen et al, Scand J Rheum 2011

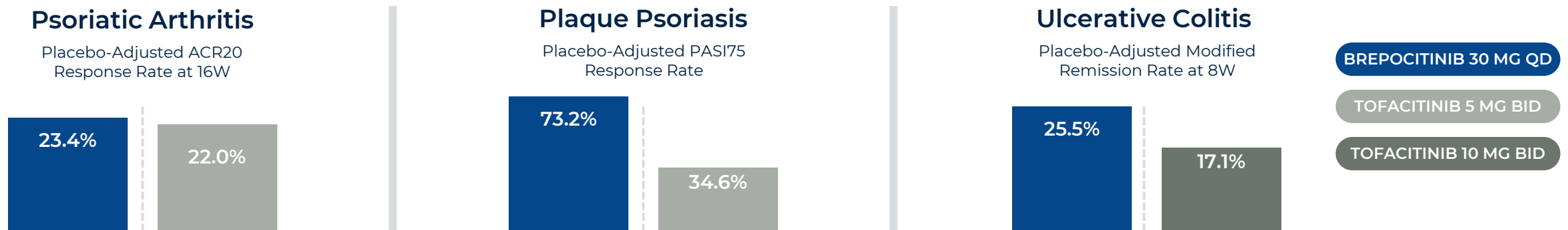
4) Tournadre et al, Arth Rheum 2012
5) Umezawa et al, Sci Reports 2018
6) Calculations based upon whole-blood inhibition assays as

reported in Dowty et al (2019) and in the Brepocitinib Investigator's Brochure. See Appendix 1 for further references.

Clinical Data Support Phase 3 Dose Selection

Cross-study comparisons of brepocitinib and tofacitinib suggest dosing brepocitinib at 30 mg daily may generate clinically meaningful efficacy in dermatomyositis

1. Tofacitinib has shown clinical efficacy in patients with DM at 5 mg twice-daily/11 mg XR doses, as demonstrated in case reports and STIR study¹
2. In large, placebo-controlled studies with comparable designs and endpoints, brepocitinib 30 mg daily has generated efficacy data that are numerically greater than those of tofacitinib 5 mg/10 mg twice-daily in other autoimmune diseases, including psoriatic arthritis, plaque psoriasis, and ulcerative colitis



No direct head-to-head data available – cross-trial comparison of studies with different inclusion-exclusion criteria and design elements

¹⁾ Paik et al, Clin Exp Rheum 2022

Psoriatic Arthritis: brepocitinib 30 mg QD (Phase 2B – 16W) vs. tofacitinib 5 mg BID (Phase 3 pooled – 12W, NCT01877668 + NCT01882439)

Plaque Psoriasis: brepocitinib 30 mg QD (Phase 2 – 12W) vs tofacitinib 5 mg BID (Phase 3 – 16W, NCT01309737)

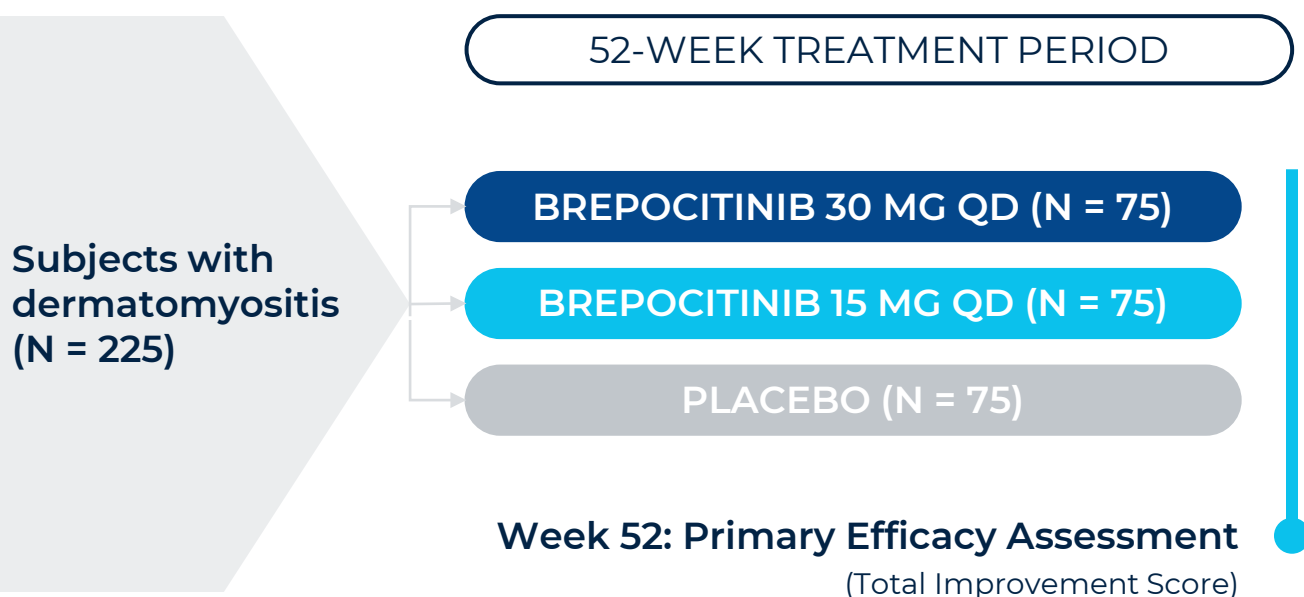
Ulcerative Colitis: brepocitinib 30 mg QD (Phase 2B – 8W) vs. tofacitinib 10 mg BID (Phase 3 – 8W, NCT01465763 + NCT01458574)

Note: Comparisons made to tofacitinib at 5 mg BID dose where available as this dose was reported mostly commonly in off-label usage in DM patients. Where more than one value is available for a competitor molecule (e.g., in the case of two Phase 3 studies), the higher value was selected for comparison to brepocitinib

DERMATOMYOSITIS

Single Phase 3 Study

Phase 3 program will evaluate 15 mg and 30 mg brepocitinib daily vs. placebo using the Total Improvement Score (TIS), a validated myositis improvement index; potential TLR in 2H 2025



Eligible Patients

Adult subjects with active dermatomyositis who are refractory or intolerant to at least one standard-of-care therapy

Primary Endpoint

Mean Total Improvement Score (TIS) at Week 52

Secondary Endpoints






- Proportion of subjects achieving TIS \geq 40 points
- Manual Muscle Testing (MMT-8)

Safety Endpoints

Incidence of treatment-emergent AEs, SAEs, AEs of special interest, clinically significant vital signs or lab abnormalities

BREPOCITINIB

Only Late-Stage Oral Therapy in Industry-Sponsored Development for DM

Molecule/Program	Sponsor	Route of Administration	Development Stage
Global Development Programs			
Brepocitinib Dual TYK2/JAK1 inhibitor		Oral, once-daily	Phase 3
OCTAGAM 10% Human immunoglobulin (IVIg)		IV Infusion	Approved
IgPro20 Human immunoglobulin		Subcutaneous infusion	Phase 3
Efgartigimod Anti-FcRn antibody fragment		Subcutaneous injection	Phase 2/3
ULTOMIRIS (ravulizumab) Anti-C5 mAb		IV Infusion	Phase 2/3
Ex-US Development Programs			
OLUMIANT (baricitinib) JAK1/2 inhibitor	Investigator-Initiated	Oral, once-daily	Phase 3 ² – France only

Includes ongoing and planned (announced) company-sponsored Phase 3 studies in dermatomyositis; excludes glucocorticoids and corticotropin injection

1) Basket study in multiple myositis subtypes (IMNM, PM, DM)

2) N = 62 patients

CONFIDENTIAL



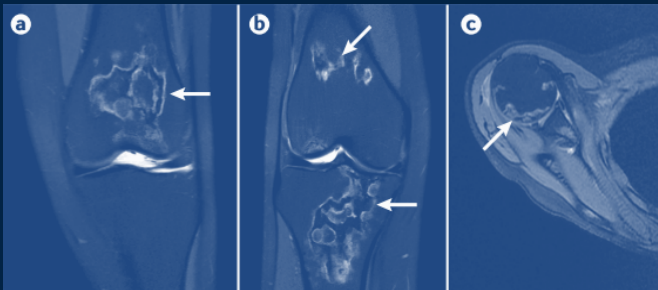
Systemic Lupus Erythematosus





MALAR (BUTTERFLY) RASH

Typical skin complication found in up to 50% of patients with SLE



OSTEONECROSIS OF JOINTS

Complication of long-term OCS use in SLE

SLE: A Heterogeneous Connective Tissue Disease

SLE is a chronic autoimmune disease characterized by elevated levels of proinflammatory cytokines, autoantibodies, and autoreactive cell types that affects up to 300,000¹ people in the United States

Clinical Presentation

Average Age of Onset	18-25 ²
Female:Male Incidence Ratio	9:1 ³
Neurological Symptoms	50% ⁴
Cutaneous and Mucosal Symptoms	70% ⁴
Gastrointestinal Symptoms	50% ⁴
Hematological Symptoms	50% ⁴
Renal Symptoms	30% ⁴
Arthritis and Musculoskeletal Symptoms	85% ⁴
10- and 15-year Mortality	9/15%⁵

Unmet Need

There are only two approved targeted agents for the treatment of SLE (Benlysta and Saphnelo)

Many treated patients fail to achieve response/remission (particularly those with moderate/severe disease)⁶

Many patients continue to experience recalcitrant organ domain-specific symptoms, and new treatments that effectively treat these manifestations are urgently needed

Images adapted from Kaul et al (2016)
 1) Centers for Disease Control
 2) Hospital for Special Surgery
 3) Weckerle et al, Clin Rev Allergy Immunol (2011)

4) Kaul et al, Nat Rev Dis Primers (2016)
 5) Kasitanon et al, Medicine (2006)
 6) Strand et al, Abstract 1077; ACR 2014

Rationale for Brepocitinib in SLE

1. Baricitinib and deucravacitinib Phase 2 studies provide clinical validation of JAK1 and TYK2 inhibition, respectively, while also highlighting need for more potent agents
2. Cross-trial comparison of brepocitinib to baricitinib and deucravacitinib in other autoimmune indications suggest potential for greater efficacy
3. Cytokine inhibition profiles further support potential for greater efficacy than baricitinib or deucravacitinib in SLE

Clinical validation of JAK1 and TYK2 inhibition in SLE has been established by baricitinib and deucravacitinib; brepocitinib's numerically better data in other indications and enhanced potency against key pathogenic cytokines suggest potential for greater efficacy

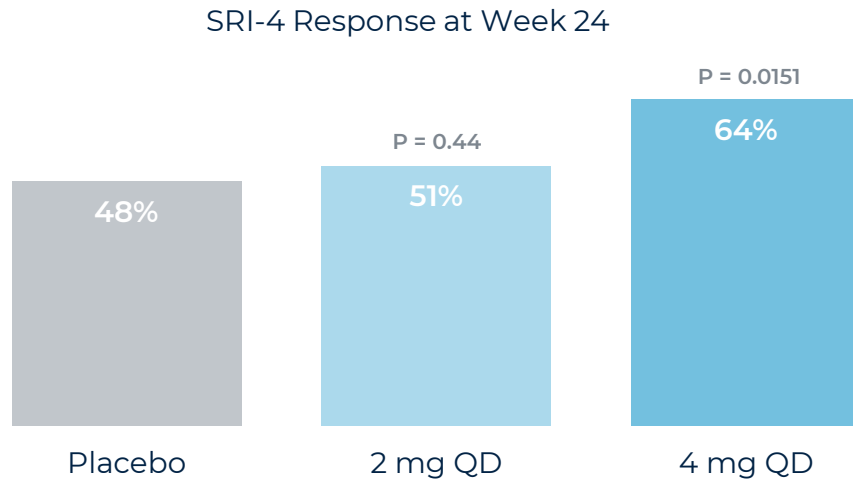
1) Wallace et al, Lancet 2018
2) EULAR 2022 Poster POS0190
3) EULAR 2022 Abstract LB0004

JAKS IN SLE

Clinical Proof-of-Concept

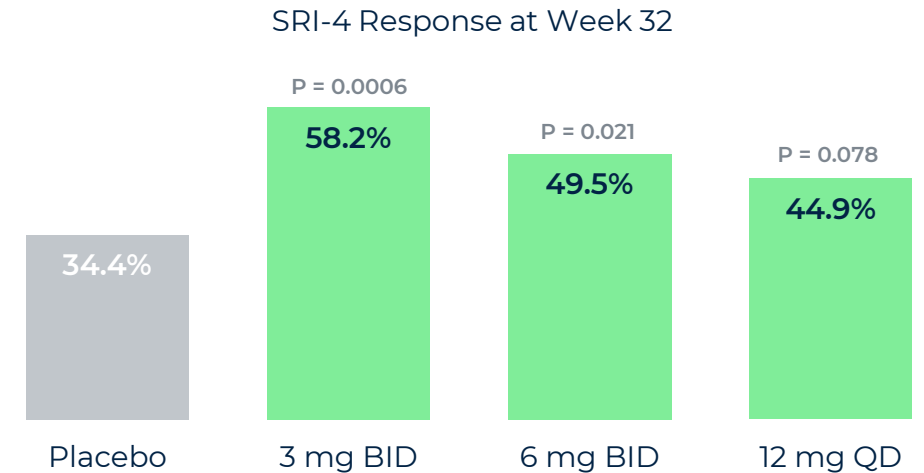
Baricitinib and deucravacitinib PoC studies established therapeutic relevance of JAK1 and TYK2 inhibition, respectively, while also highlighting need for more potent agents

Phase 2 Study of Baricitinib in SLE¹



One of two phase 3 confirmatory studies achieved statistically significant efficacy on primary endpoint of SRI-4 at Week 52, with 56.7% of patients who received 4 mg QD achieving response compared to 45.9% of patients who received placebo²

Phase 2 Study of Deucravacitinib in SLE³



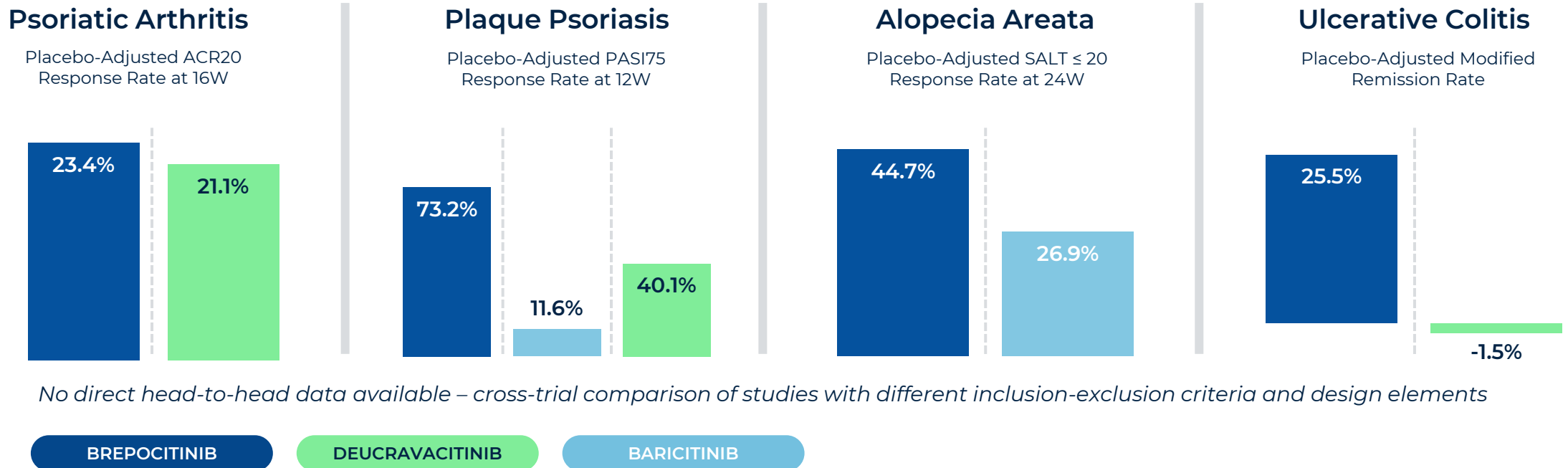
Primary endpoint of SRI-4 response at Week 32 was met at 3 mg BID and 6 mg BID dose levels; 12 mg QD did not achieve significance

1) Wallace et al, The Lancet (2018)
2) EULAR 2022 Poster POS0190
3) EULAR 2022 Abstract LB0004

POTENTIAL FOR GREATER EFFICACY

Clinical Data From Other Autoimmune Indications

In large, placebo-controlled studies with comparable designs in other indications, brepocitinib has generated efficacy data that are numerically greater than those of baricitinib and deucravacitinib on registrational endpoints



No direct head-to-head data available – cross-trial comparison of studies with different inclusion-exclusion criteria and design elements

Psoriatic Arthritis: brepocitinib 30 mg QD (Phase 2B – 16W) vs. deucravacitinib 6 mg QD (Phase 2 – 16W, NCT03881059)
Plaque Psoriasis: brepocitinib 30 mg QD (Phase 2 – 12W) vs. baricitinib 4 mg QD (Phase 2B – 12W, NCT01490632) vs. deucravacitinib 6 mg QD (Phase 3 POETYK-PSO-2 – 12W, NCT03611751)
Alopecia Areata: brepocitinib 60 mg QD/30 mg QD (Phase 2 – 24W) vs. baricitinib 4 mg QD (Phase 3 BRAVE-AA2 – 24W, NCT03899259)
Ulcerative Colitis: brepocitinib 30 mg QD (Phase 2B – 8W) vs. deucravacitinib 6 mg BID (Phase 2 LATTICE-UC – 12W, NCT03934216)

Note: where more than one value is available for a competitor molecule (e.g., in the case of two Phase 3 studies), the higher value was selected for comparison to brepocitinib

POTENTIAL FOR GREATER EFFICACY

Comparative Inhibition Of Type I IFN

There is substantial evidence that SLE is a type I interferon-driven disease; brepocitinib's dual inhibition of TYK2 and JAK1 may provide best-in-class type I IFN suppression

Type I IFN is the key pathogenic cytokine in SLE

A type I interferon gene signature is present in 50-75% of adult SLE patients and up to 90% of pediatric patients¹

SLE disease activity correlates with IFN- α levels and the strength of the IFN gene signature^{2,3}

Type I IFNs are secreted by pDCs and encourage presentation of self-antigen to T-cells and expansion of autoreactive B-cells, creating a self-sustaining pattern of interferon activation, chronic inflammation, and tissue destruction⁴

The recent FDA approval of SAPHNELO (anifrolumab), a monoclonal antibody inhibitor of the type I interferon receptor⁵, underscores the therapeutic relevance of interferon modulation in SLE treatment

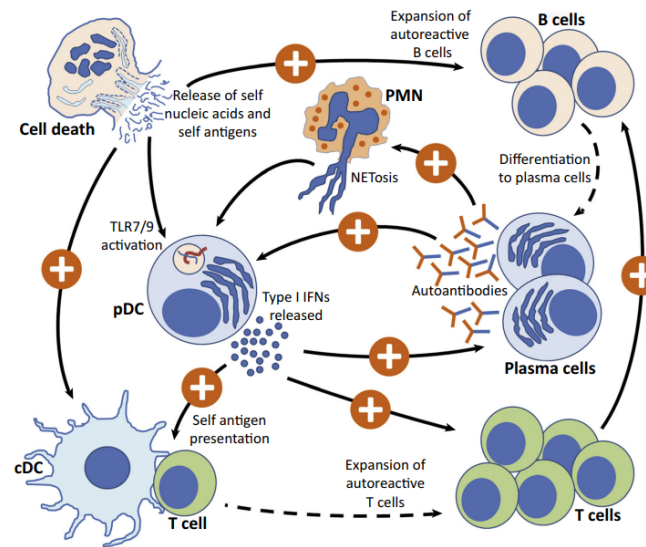
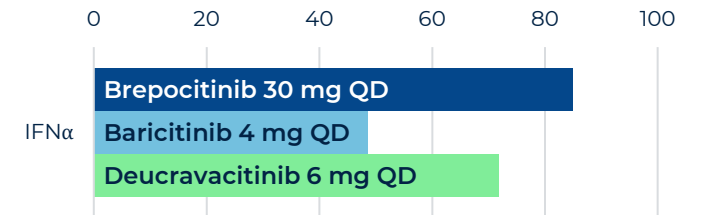


Figure adapted from Ganguly (2017)

Whole blood assays suggest brepocitinib may provide best-in-class suppression of type I IFN

Percent Cytokine Inhibition at Modeled Exposures⁸



Cross-study comparisons with different assay conditions

Identification of catalytically-deficient TYK2 and JAK1 mutants with full IFN signaling competency suggests inhibition of both TYK2 and JAK1 is required for maximal type I IFN suppression⁶

Deucravacitinib, as a highly selective allosteric inhibitor of TYK2, does not inhibit JAK1⁷

1) Ronnblom and Leonard, Lupus Sci Med (2019)
 2) Bengtsson et al, Lupus (2000)
 3) Feng et al, Arth Rheum (2006)
 4) Ganguly, Trends In Immunol (2017)

5) SAPHNELO FDA Label
 6) Li et al, J Immunol (2013)
 7) Chimalakonda et al, Dermatol Ther (2021)
 8) Calculations based upon whole-blood inhibition assays as

reported in Dowty et al (2019) and in the Brepocitinib Investigator's Brochure. See Appendix 1 for further references.

POTENTIAL FOR GREATER EFFICACY

Comparative Inhibition Of Other Pathogenic TYK2- and JAK1-Mediated Cytokines

In addition to type I interferon, brepocitinib inhibits several other inflammatory cytokines that contribute to SLE pathophysiology

Other key cytokines: IFN γ , IL-6, IL-12, and IL-23

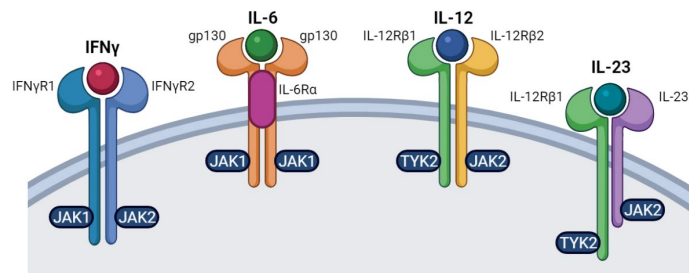
IFN γ : Upregulated in the plasma of patients with SLE; correlates strongly with type I IFN upregulation¹; high IFN γ activity is associated with nephritis and arthritis¹

IL-6: Serum IL-6 levels are higher in SLE patients than in healthy controls; IL-6 levels correlate positively with disease activity²

IL-12: Elevated in plasma of SLE patients compared to healthy controls³; IL-12p40 subunit expression correlates with disease activity⁴

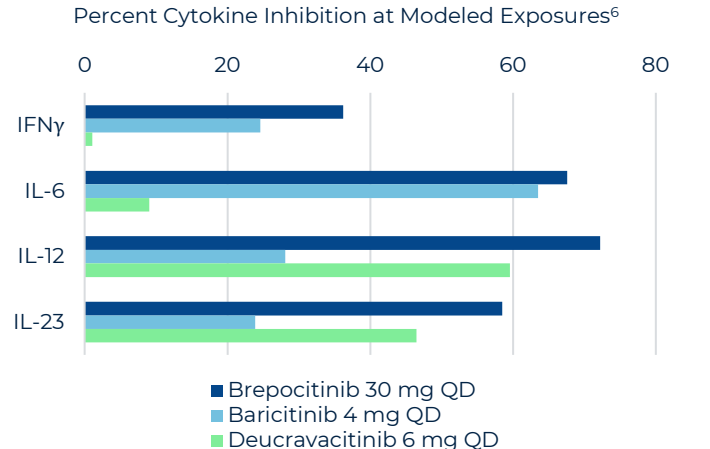
IL-23: Elevated in the serum of patients with SLE; correlates positively with skin and nephritis symptoms⁵

IFN γ , IL-6, IL-12, and IL-23 signaling is mediated by JAKs inhibited by brepocitinib



Brepocitinib's potent inhibition of TYK2 and JAK1 is expected to result in substantial inhibition of IFN γ , IL-6, IL-12, and IL-23 signaling activity

Whole blood assays suggest brepocitinib may provide best-in-class suppression of IFN γ , IL-6, IL-12, and IL-23



Cross-study comparisons with different assay conditions

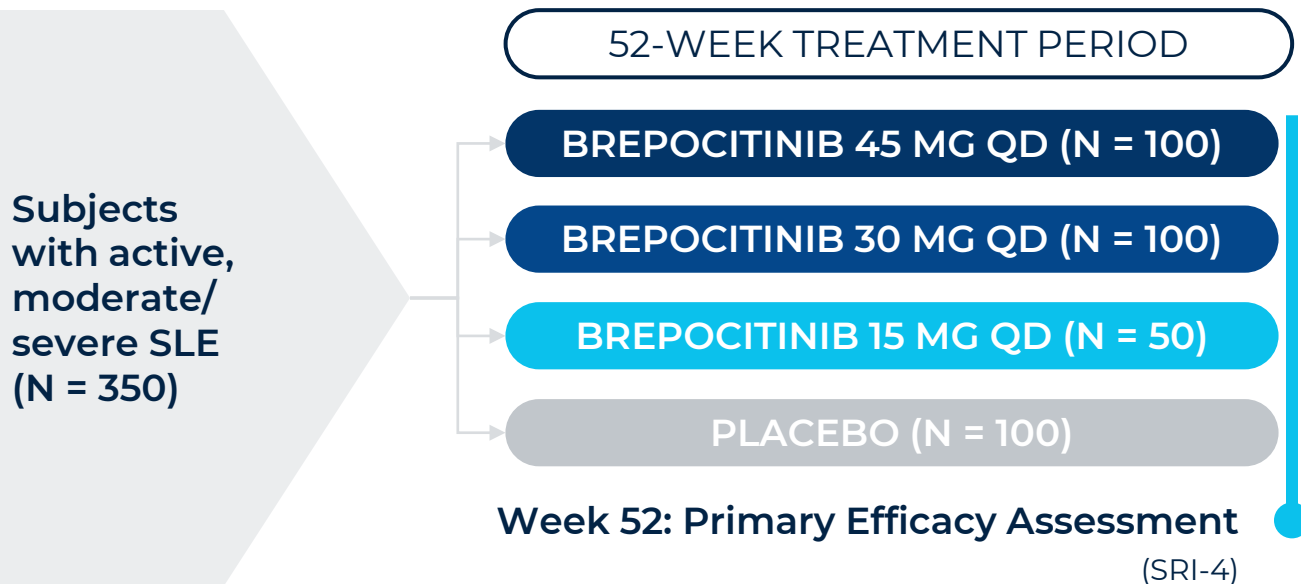
1) Oke et al, Arth Res Ther (2019)
2) Ding et al, Clinics (2020)
3) Talaat et al, Cytokine (2015)
4) Lauwerys et al, Lupus (2002)

5) Vukelic et al, Lupus (2020)
6) Calculations based upon whole-blood inhibition assays as reported in Dowty et al (2019) and in the Brepocitinib Investigator's Brochure. See Appendix 1 for further references.

ONGOING

Phase 2B Study in SLE

Large phase 2B study was designed to serve as 1 of 2 potential registration-enabling studies; primary endpoint is SRI-4, a validated SLE improvement index; top-line data anticipated in 2H 2023



Eligible Patients

Adult subjects with moderate to severe active lupus who are receiving a stable regimen of SOC immunosuppressive agents

Primary Endpoint

Systemic Lupus Responder Index change of 4 (SRI-4) at Week 52









Secondary Endpoints

- Time to first severe flare
- Lupus Low Disease Activity State (LLDAS)
- Reduction in steroid usage
- Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI-A) response

Safety Endpoints

Incidence of treatment-emergent AEs, SAEs, AEs of special interest, clinically significant vital signs or lab abnormalities

Key Competitive Landscape in SLE

Molecule/Program	Sponsor	Route of Administration	Development Stage
Orals			
Brepocitinib TYK2/JAK1 inhibitor	 priosant	Oral, once-daily	Phase 2B
Deucravacitinib Allosteric TYK2 inhibitor	 Bristol Myers Squibb	Oral, once/twice-daily	Entering Phase 3 ¹
Cenerimod S1P1 Receptor Modulator	 idorsia	Oral, once-daily	Entering Phase 3 ²
Upadacitinib JAK1 inhibitor	 abbvie	Oral, once-daily	Phase 2
Biologics			
Obinutuzumab Anti-CD20 mAb	 Roche	IV Infusion	Phase 3
Litifilimab Anti-BDCA2 mAb	 Biogen	SC injection	Phase 3
Dapirolizumab pegol Anti-CD40L mAb	 ucb Pharma	IV Infusion	Phase 3
Telitacicept Anti-BLyS/APRIL mAb	 RemeGen	SC injection	Phase 3

Source: Global Data; list of competitive programs is not exhaustive

1) BMS Q1 '22 Earnings Release

2) Idorsia Press Release, Nov 1, 2021

Other Indication Overviews: HS & NIU





HIDRADENITIS SUPPURATIVA

Extensive skin involvement with fistula (tunnel) formation and scarring in a Hurley Stage III patient

HIDRADENITIS SUPPURATIVA (HS)

A Severe, Disfiguring Inflammatory Skin Disease

HS is an inflammatory skin disease characterized by the formation of painful nodules and abscesses in intertriginous zones (skin folds) that affects approximately 170,000 individuals in the United States¹¹

Clinical Presentation

Peak age of onset	18-29 years ¹
Female:Male Incidence Ratio	3:1 ²
Key Symptoms	Nodule and abscess formation Tissue destruction, scarring Purulent, malodorous discharge Pain
Hurley Stage ³	Hurley I (mild): 50% Hurley II (moderate): 35% Hurley III (severe): 15%
Comorbidities	Metabolic syndrome⁴ Spondylarthritis² Inflammatory bowel disease⁵

Unmet Need

HS is an exceptionally burdensome disease, with patients experiencing highest-measured levels of skin-related QoL issues⁶, markedly elevated rates of depression⁷, and suicide risk >2x higher than the general population⁸

Humira (adalimumab) is the only approved targeted therapy for HS, and only ~50% of moderate/severe patients will respond⁹

Surgical intervention in HS is generally considered an option of last resort, as wide excision is a major procedure often requiring significant reconstruction¹⁰

1) Ingram, Br J Dermatol (2020)
 2) Shlyankevich et al, J Am Acad Derm (2014)
 3) Based on Conouli-Poitrine et al, J Am Acad Derm (2009)
 4) Sabat et al, PLoS One (2012)
 5) Deckers et al, J Am Acad Derm (2017)
 6) Von Der Werth, Br J Dermatol 2001

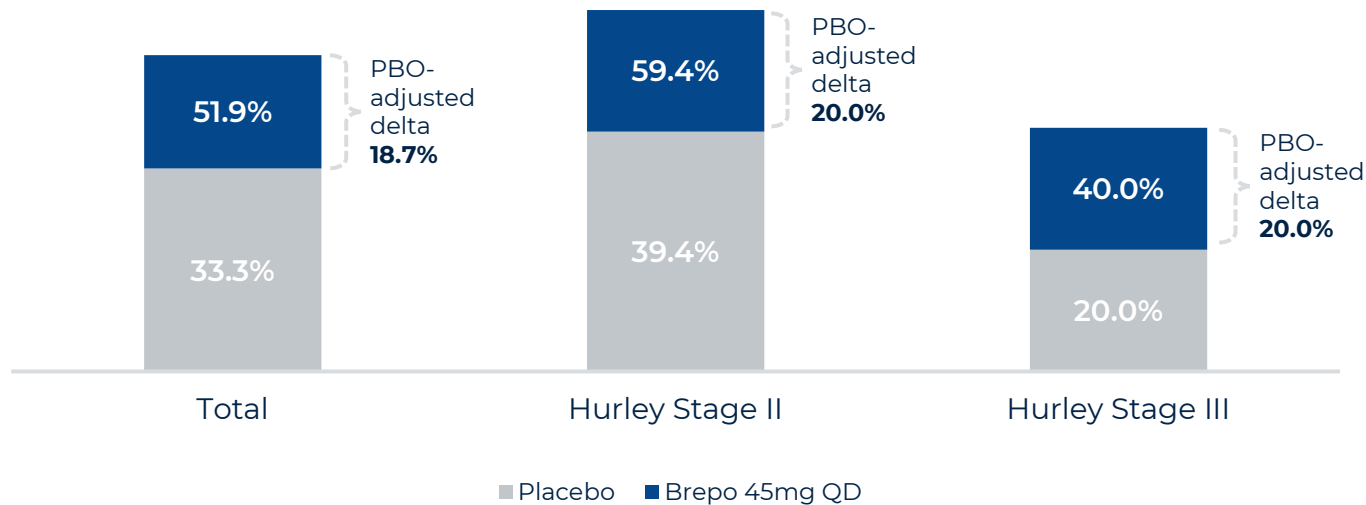
7) Kurek et al, Dtsch Dermatol Ges 2013
 8) Thorlacious et al, J Invest Dermatol 2018
 9) Kimball et al, NEJM 2016
 10) Alharbi et al, BMC Dermatol (2012)
 11) Estimates for moderate/severe HS only based on Phan et al, Biomed Derm 2020

BREPOCITINIB IN HS

Clinical Proof-of-Concept

In a 16-week study of brepocitinib in 100 patients with moderate-to-severe hidradenitis suppurativa, brepocitinib was associated with a significantly higher HiSCR response rate than placebo

Patients Achieving HiSCR Response at Week 16
Response Rate by Hurley Stage



27 of 52 (51.9%) brepocitinib-treated patients achieved HiSCR compared to 16 of 48 (33.3%) placebo-treated patients ($p = 0.0298$)

Effect sizes were consistent across Hurley stages and among patients who had previously demonstrated inadequate response to TNF inhibitors

Key secondary endpoints, including total AN count and time to first flare, also achieved statistical significance

Cytokine Pathogenicity in HS Suggests Best-In-Class Potential for Brepocitinib

Hidradenitis suppurativa is associated with dysregulations in TYK2- and JAK1-linked cytokine signaling pathways

Cytokine Pathogenicity and Putative Effects in HS Patients

Type II IFN (γ)	<ul style="list-style-type: none"> Elevated in wound exudate from HS patients¹ Elevated gene expression in HS lesional skin² Upregulated IFNγ expression leads to increased Th1 polarization and induction of Th1-attracting chemokines, contributing to immune infiltration from the bloodstream³
IL-12	<ul style="list-style-type: none"> Elevated transcript expression in HS lesions (at levels exceeding those in psoriasis lesions)⁴ Elevated protein expression in HS lesional skin⁵ Secreted by lesion-infiltrating macrophages following TLR stimulation by microbial agents⁶
IL-23	<ul style="list-style-type: none"> Elevated transcript expression in HS lesions⁴ Secreted by lesion-infiltrating macrophages following TLR stimulation by microbial agents⁶ Supports Th17 cell activation and secretion of IL-17, which contributes to chemokine gradient and enhancement of immune cell infiltration³

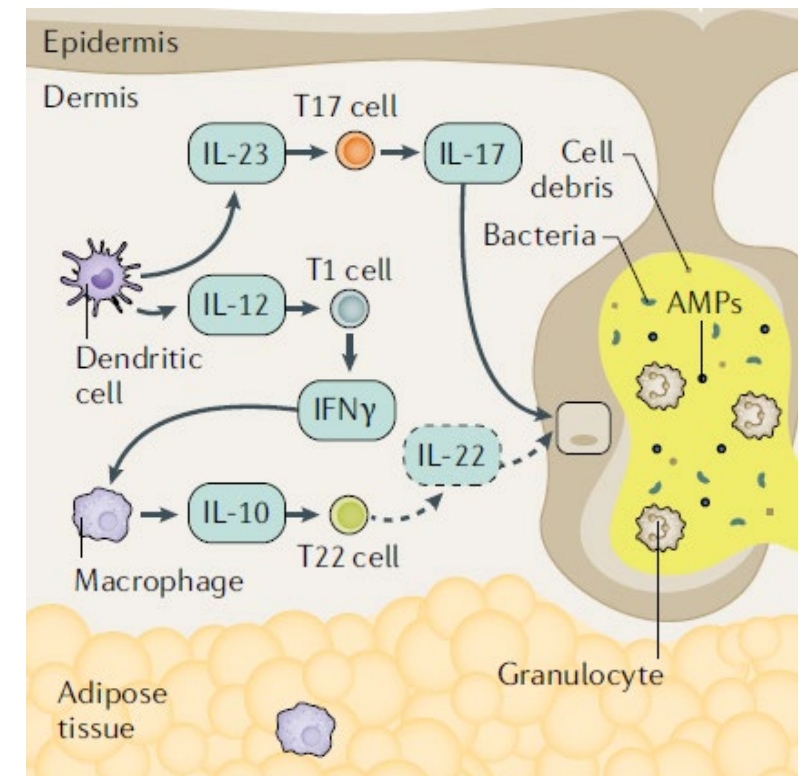
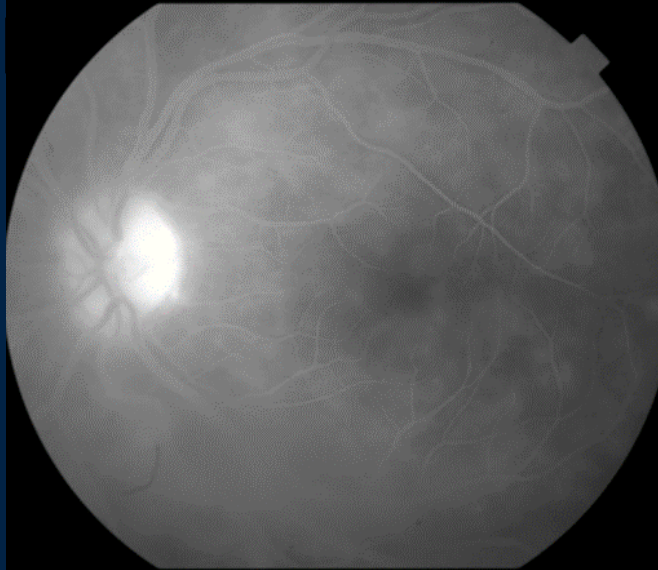


Figure adapted from Sabat et al, Nat Rev Dis Primers 2020

1) Banerjee et al, Immunol Invest 2017
 2) Hotz et al, Invest Dermatol 2016
 3) Sabat et al, Nat Rev Dis Primer 2020

4) Wolk et al, J Immunol 2011
 5) Vossen et al, Allergy 2018
 6) Schlapbach et al, J Am Acad Derm 2011



POSTERIOR SEGMENT INFLAMMATION

Illustrative fluorescein angiography image indicating diffuse areas of capillary leakage and disc hyperfluorescence

NON-INFECTIOUS UVEITIS (NIU) A Sight-Threatening Ocular Disease

Non-anterior NIU is a chronic autoimmune disease characterized by intraocular inflammation that affects approximately 75,000¹ people in the United States

Clinical Presentation

Peak Age of Onset **17-60 years²**

Key Symptoms **Light sensitivity, pain, redness, floaters**

Associated Systemic Diseases⁴ **Beçhet disease, Multiple sclerosis, Spondyloarthropathies, Connective tissue diseases**

Location of Inflammation **Intermediate uveitis: 4%¹
Posterior uveitis: 43%¹
Pan-uveitis: 52%¹**

Visual Impairment **Unilateral visual impairment: 16%³
Bilateral visual impairment: 9%³
Unilateral legal blindness: 18%³
Bilateral legal blindness: 6%³**

Unmet Need

Up to 70% of patients with uveitis experience some degree of vision loss⁴, with up to 18% experiencing some degree of blindness³

Humira (adalimumab) is the only approved targeted therapy for NIU, and many patients fail to respond adequately⁵

Certain disease manifestations are not adequately treated with adalimumab (e.g., macular edema)⁶, suggesting that additional treatment options for specific symptoms are needed

1) PriovantTx estimates based on Thorne et al, JAMA Ophthalmol. (2016)
2) Barisani-Asenbauer 2012
3) Rothova et al, Br J Ophthalmol (1996)

4) De Smet et al, Prog in Ret and Eye Res (2011)
5) Jaffet et al, NEJM (2016)
6) Androudi et al, Ophthalmology (2010)
Image adapted from from Sadiq et al (2020)

JAKS IN NIU

Clinical Proof-of-Concept

Phase 2 study of filgotinib (JAK1), which showed statistically significant benefit, provides proof-of-concept for potential therapeutic relevance of JAK1 inhibition in NIU

Filgotinib Phase 2 Results

HUMBOLDT

Endpoint	Filgotinib (n=32)	Placebo (n=34)	Statistics (95% CI)
Week 24 % failure ¹	37.5%	67.6%	Δ 30.1% (-56.2, -4.1) P=0.0064

Filgotinib's Phase 2 study suggests JAK1 inhibition may be effective in NIU, with results comparable to those achieved by Humira

Brepocitinib's enhanced potency against key NIU cytokines (including those whose signaling is mediated by TYK2) suggests there is potential for greater efficacy

1) Failure defined as new lesion or worsening of BCVA by 15 letters, or inability to achieve ACC and VH grade of 0.5+ by Week 6, or a 2-step increase in ACC or VH grade after week 6 (see NIU Appendix for additional details).

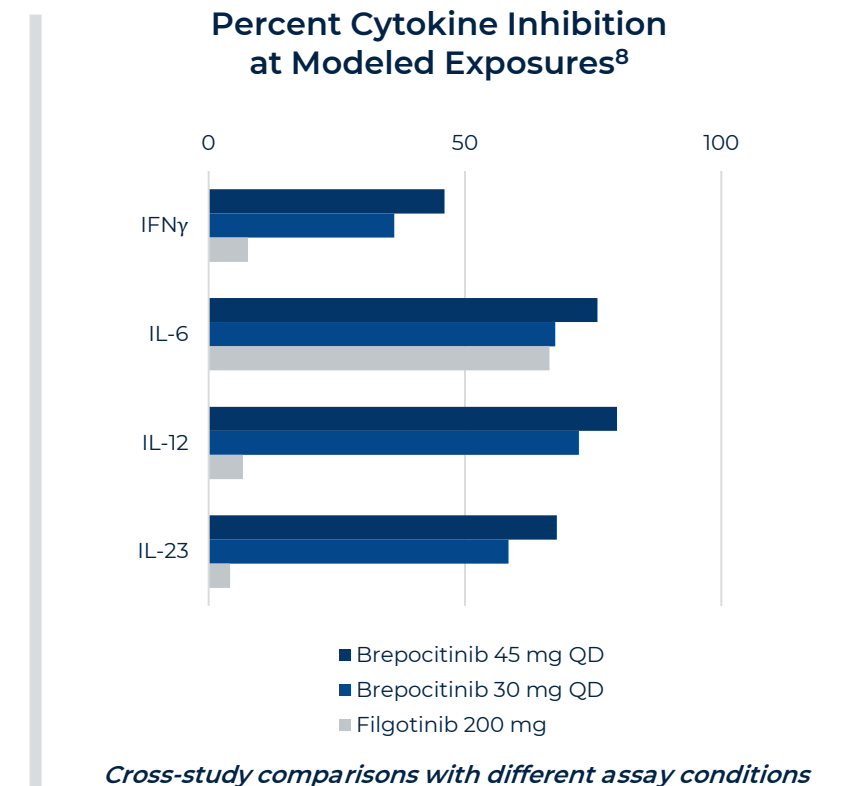
2) Assumes dropouts are not treatment failures, if assume all dropouts are failures, rates are 0.62 and 0.82, respectively.

Brepocitinib Potential For Greater Efficacy vs. Filgotinib

Brepocitinib is a more potent inhibitor than filgotinib of multiple cytokines that play a key role in NIU

Cytokine Pathogenicity and Putative Effects in NIU Patients

Type II IFN (γ)	<ul style="list-style-type: none"> Aqueous and serum samples from uveitis patients showed higher levels of IFNγ than matched healthy controls¹ High IFNγ expression associated with increased loss of vision¹
IL-6	<ul style="list-style-type: none"> IL-6 levels are higher in NIU patient serum² and vitreous³ than in healthy controls Serum IL-6 levels are higher in NIU patients with active disease than those in remission² Contributes to immune dysregulation in NIU by promoting differentiation of naïve T cells into Th17 effector cells⁴
IL-12	<ul style="list-style-type: none"> IL-12 levels are higher in uveitis patient vitreous than healthy controls and were higher in patients with active disease compared to those in remission⁵
IL-23	<ul style="list-style-type: none"> Increased IL-23 has been found in the serum and PBMC supernatant of patients with VKH and Bechet uveitis compared to healthy controls and patients with inactive uveitis⁶ Elevated IL-23 production in the vitreous of posterior NIU patients has been observed compared to healthy controls⁷



1) Lacomba et al, Arch Ophthalmol (2000)
 2) Kramer et al, Curr Eye Res (2007)
 3) De Boer et al, Curr Eye Res (1992)
 4) Mesquida et al, Clin Exp Immunol (2014)

5) El-Shawbrawi et al, Am Acad Ophthalmol (1998)
 6) Pepple and Lin, Ophthalmol (2019)
 7) Velez et al, JAMA Ophthalmol (2016)
 8) Calculations based upon whole-blood inhibition assays as

reported in Dowty et al (2019) and in the Brepocitinib Investigator's Brochure. See Appendix 1 for further references.

The logo for Priovent Therapeutics features the word "priovent" in a dark blue, lowercase, sans-serif font. The letter "i" is replaced by a stylized graphic of two light blue circles connected by a thin line, resembling a molecular structure. Below "priovent", the word "therapeutics" is written in a smaller, light blue, lowercase, sans-serif font, with wide letter spacing.

priovent
therapeutics

APPENDIX 1

Additional References

Slide 5: Clinical Program and Safety Overview

TEAEs Incidence Rate Chart

Brepocitinib source data: Brepocitinib Clinical Study Reports (Prioivant data on file)

Tofacitinib source data: Pfizer ORAL Surveillance Study (malignancy, MACE); Cohen et al (2020) (thrombosis, serious infections, and herpes zoster)

Baricitinib source data: FDA Risk Review (May 2018) (thrombosis); Smolen et al (2019) (malignancy, MACE, serious infections, herpes zoster)

Upadacitinib source data: FDA Risk Review (Aug 2019)

Multiple Slides: Comparative Cytokine Inhibition

Cytokine Inhibition at Modeled Therapeutic Exposures

Methodology: Using the modeling approach described in Dowty et al, Pharmacol Res Perspect (2019), estimated IC_{xx} (% levels of cytokine inhibition) values were calculated for brepocitinib, tofacitinib, baricitinib, upadacitinib, deucravacitinib, and filgotinib at various therapeutic dose levels.

Brepocitinib source data: Brepocitinib Investigator's Brochure; Prioivant data on file

Tofacitinib source data: Dowty et al, Pharmacol Res Perspect (2019); Dowty et al, J Pharmacol Exp Ther (2013)

Baricitinib source data: Dowty et al, Pharmacol Res Perspect (2019)

Upadacitinib source data: Dowty et al, Pharmacol Res Perspect (2019); EMA Risk Assessment Report – RINVOQ (June 2021)

Deucravacitinib source data: Prioivant data on file; Chimalakonda et al, Dermatol Ther (2021); Wroblewski et al, J Med Chem (2019)

Filgotinib source data: Dowty et al, Pharmacol Res Perspect (2019); Scholze et al, PLoS ONE (2014)