

# Introduction to Priovent

November 2023



# 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 six placebo-controlled studies completed to-date with oral formulation (once-daily administration)

**Well-Characterized Safety Profile:** Exposure in >1,400 subjects and patients suggests safety profile consistent with approved JAK inhibitors

**Distinctive Strategy:** Orphan and specialty autoimmune franchise across diseases with high morbidity and mortality, few approved therapies (including no JAKi), and pathobiologies for which both TYK2 and JAK1 inhibition are expected to contribute to efficacy

**Ongoing Registrational Program in DM:** Single registrational phase 3 study in dermatomyositis (DM) with data expected in 2025, potential product launch in 2026

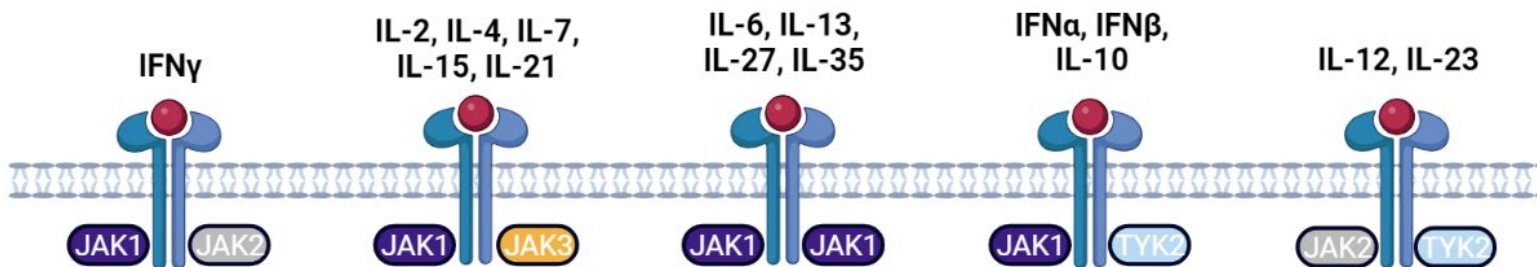
## ORAL BREPOCITINIB

# Optimized Pharmacology for Highly Inflammatory Diseases with Multiple Pathogenic Cytokines

Key insight:  
different JAKs for  
different diseases

**Different diseases are driven by different combinations of cytokines, requiring inhibition of specific JAK isoforms to treat distinct indications most effectively**

Field is currently  
focused on single  
isoform inhibitors  
(specifically  
TYK2 or JAK1)



JAK1 coverage – Rinvog, Cibinqo

TYK2 coverage – Sotyktu

Greater coverage  
vs. TYK2s

Dual Hit

Greater coverage  
vs. JAK1s

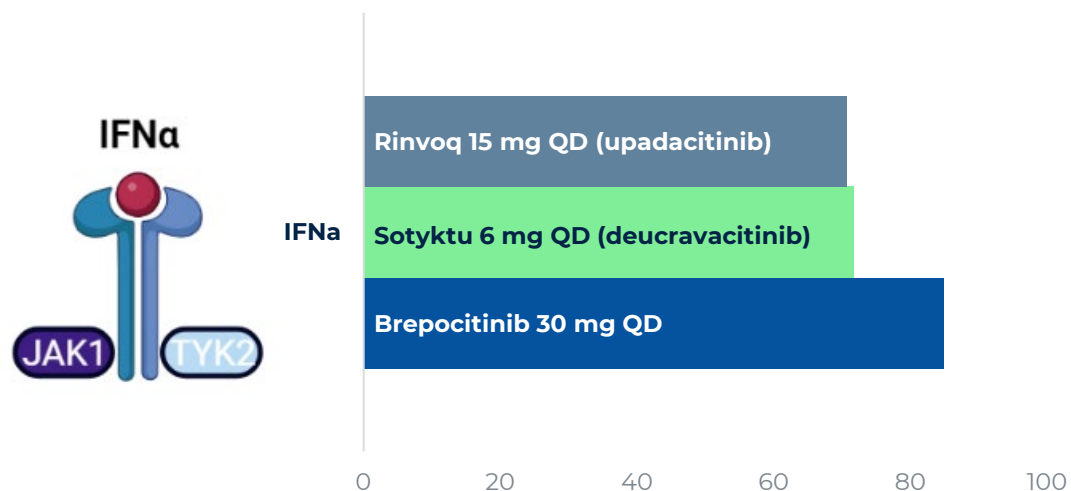
Brepocitinib was  
designed to target  
both TYK2 and JAK1

**Hypothesis:**  
brepocitinib can provide  
best-in-class efficacy in  
indications mediated by  
the TYK2/JAK1 dimer and  
in diseases requiring  
broad cytokine coverage

# In Vitro Data Support Mechanistic Benefits of Dual Inhibition of TYK2 and JAK1

## Dual Hit

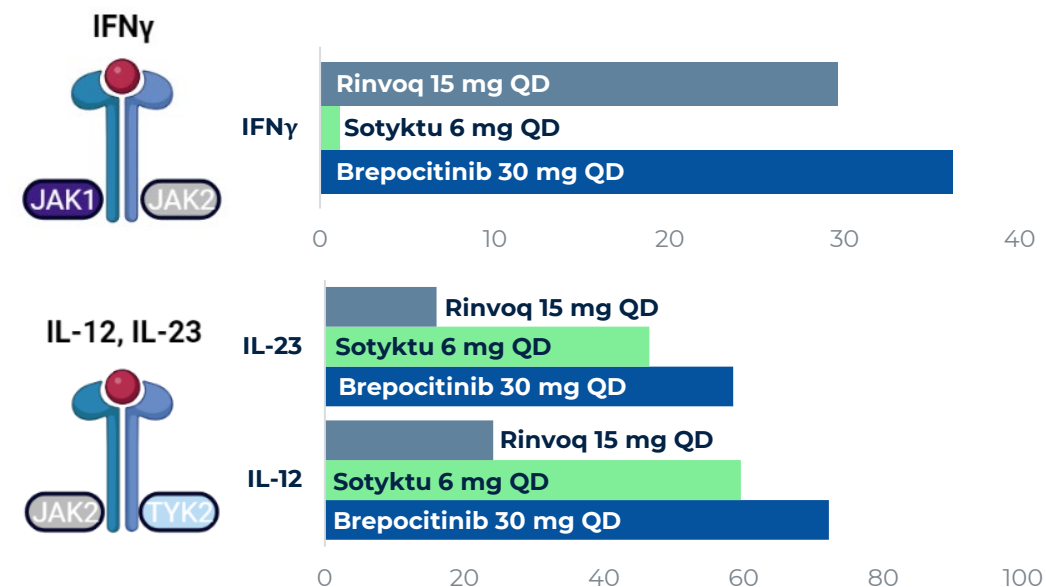
Percent Cytokine Inhibition at Modeled Exposures<sup>1</sup>



Brepocitinib may be able to achieve deeper Type I IFN suppression than is possible by targeting either TYK2 or JAK1 alone

## Greater Coverage

Percent Cytokine Inhibition at Modeled Exposures<sup>1</sup>



Brepocitinib may recapitulate in a single molecule the cytokine suppression profiles of both the leading TYK2 and JAK1 agents

1) Figures reflect data generated from separate in vitro assays performed by Pfizer

## ORAL BREPOCITINIB

# Statistically Significant and Clinically Meaningful Results in Six Completed Phase 2 Studies

Study Population	N <sup>1</sup>	Brepocitinib Dose	Primary Endpoint Result	Statistical Significance
<b>Psoriatic Arthritis</b> Patients with active PsA	218	30 mg once daily	23.4% placebo-adjusted ACR20 RR at week 16	<b>P = 0.0197</b>
<b>Plaque Psoriasis</b> Patients with moderate-to-severe PsO	212	30 mg once daily	-10.1 placebo-adjusted CFB in PASI Score at week 12	<b>P &lt; 0.0001</b>
<b>Ulcerative Colitis</b> Patients with moderate-to-severe UC	167	30 mg once daily	-2.28 placebo-adjusted CFB in Mayo Score at week 8	<b>P = 0.0005</b>
<b>Alopecia Areata</b> Patients with moderate-to-severe AA	94 <sup>2</sup>	30 mg once daily <sup>3</sup>	49.18 placebo-adjusted CFB in SALT Score at week 24	<b>P &lt; 0.0001<sup>4</sup></b>
<b>Hidradenitis Suppurativa</b> Patients with moderate-to-severe HS	100	45 mg once daily <sup>5</sup>	18.7% placebo-adjusted HiSCR Rate at week 16	<b>P = 0.0298<sup>4</sup></b>
<b>Crohn's Disease</b> Patients with moderate-to-severe CD	151	60 mg once daily <sup>6</sup>	21.4% placebo-adjusted SES-CD 50 Rate at week 12	<b>P = 0.0012<sup>4</sup></b>

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

6) Brepocitinib 60 mg once daily was the only brepocitinib dose evaluated in this study  
CFB: change from baseline; RR: response rate

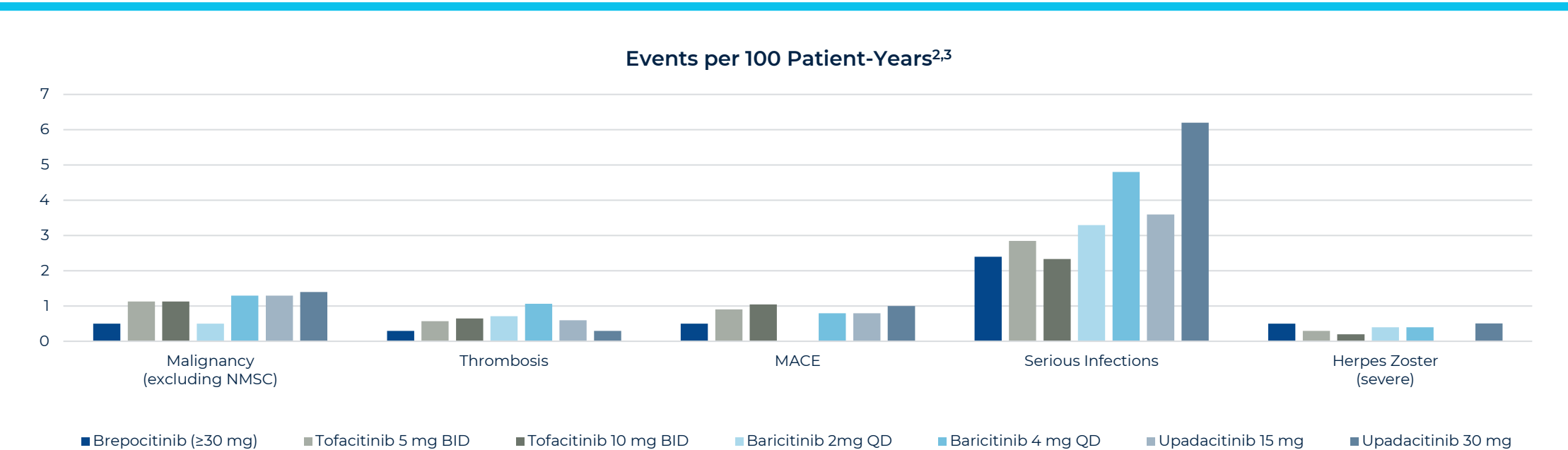
# ORAL BREPOCITINIB

## Safety Overview

Clinical experience in more than 1,400<sup>1</sup> exposed subjects and patients suggests a safety profile consistent with those of approved JAK inhibitors

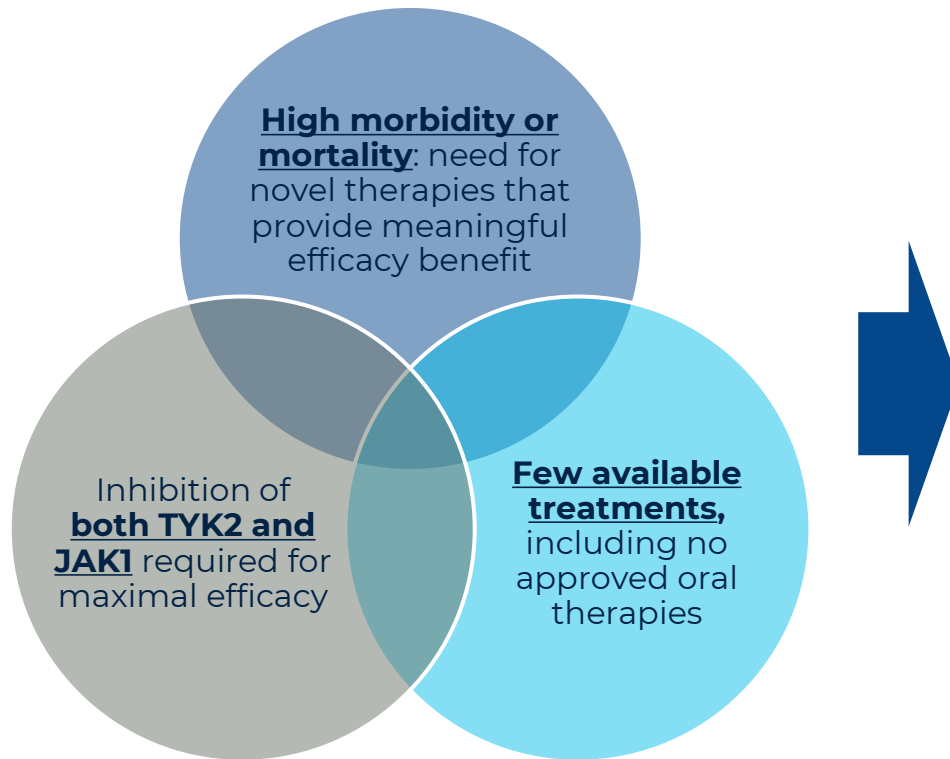
### Comparable Incidence Rates of TEAEs of Interest vs. Approved JAKs

*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. Brepocitinib ≥30 mg comprises over 90% of aggregated patient-years of brepocitinib 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 Focus: Indications with High Unmet Need and Tailored to Novel Mechanism of Dual TYK2/JAK1 Inhibition



## Ongoing Registrational Program

### Dermatomyositis

- Large orphan indication with no NCEs approved in past 60 years and no other oral therapies in late-stage development
- Registrational phase 3 study ongoing – TLR expected in 2025

## Potential Expansion Opportunities

### Hidradenitis Suppurativa

- Phase 2 results suggest potential for better efficacy than selective JAK1 inhibitors and comparable to leading biologics

### Non-Infectious Uveitis

- PoC data expected Q1 2024



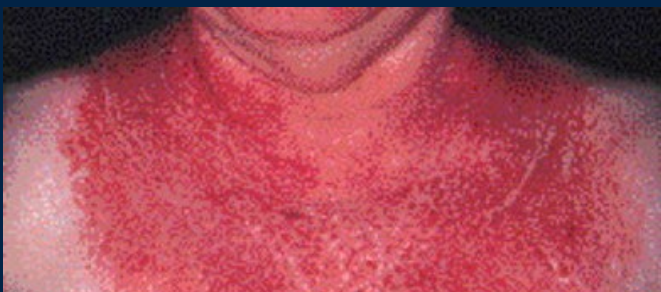
# Dermatomyositis





### 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 37,000<sup>1</sup> adults in the United States

10-40%

Mortality at five years<sup>2</sup>

100%

Red, painful, itchy skin rash often disseminated across substantial body surface area

88%

Proximal muscle weakness<sup>3</sup>, limiting activities of daily living (ADL)

42%

Interstitial lung disease<sup>4</sup>, contributing to substantial morbidity

0

Other oral therapies in industry-sponsored late-stage development<sup>5</sup>

0

NCEs approved in last 60 years

1) PrioventTx estimates based on Reeder 2010, Smoyer-Tomic 2012, and claims analysis  
 2) Liu et al, Oncol Letters (2018)  
 3) Fardet et al, Medicine (2009)  
 4) Sun et al, Sem Arth Rheum (2021)  
 5) Phase 3 trials or adaptive Phase 2/3 trials

# Dermatomyositis Prevalence

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

**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



**Priovant Claims Analysis**  
Analysis of Komodo claims database from 2016-2020

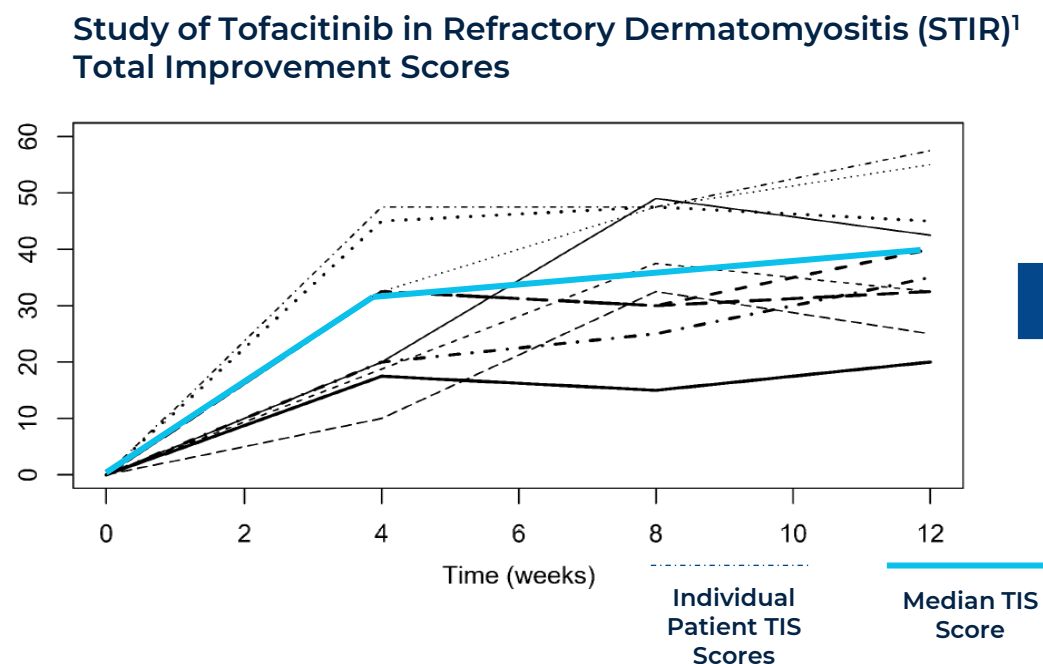


A prevalence rate of **~14/100,000** individuals implies approximately **37,000** adult patients in the United States with dermatomyositis

## JAK INHIBITION IN DERMATOMYOSITIS

# Clinical Proof-of-Concept with Tofacitinib

Investigator-initiated open-label study of tofacitinib in refractory dermatomyositis demonstrated activity comparable to that of IVIg, the only approved non-corticosteroid/corticotropin therapy for dermatomyositis



### STIR Study TIS Outcomes

*Open-label, single-arm*

**100%**

TIS20 Response Rate at Week 12

**40**

Median TIS Score at Week 12<sup>3</sup>

### ProDERM Phase 3 Study (IVIg)<sup>2</sup> TIS Outcomes

*Double-blind, placebo-controlled*

**79%**

TIS20 Response Rate at Week 16

**43**

Mean TIS Score at Week 12<sup>3</sup>

*Cross-study comparison; no head-to-head data available*

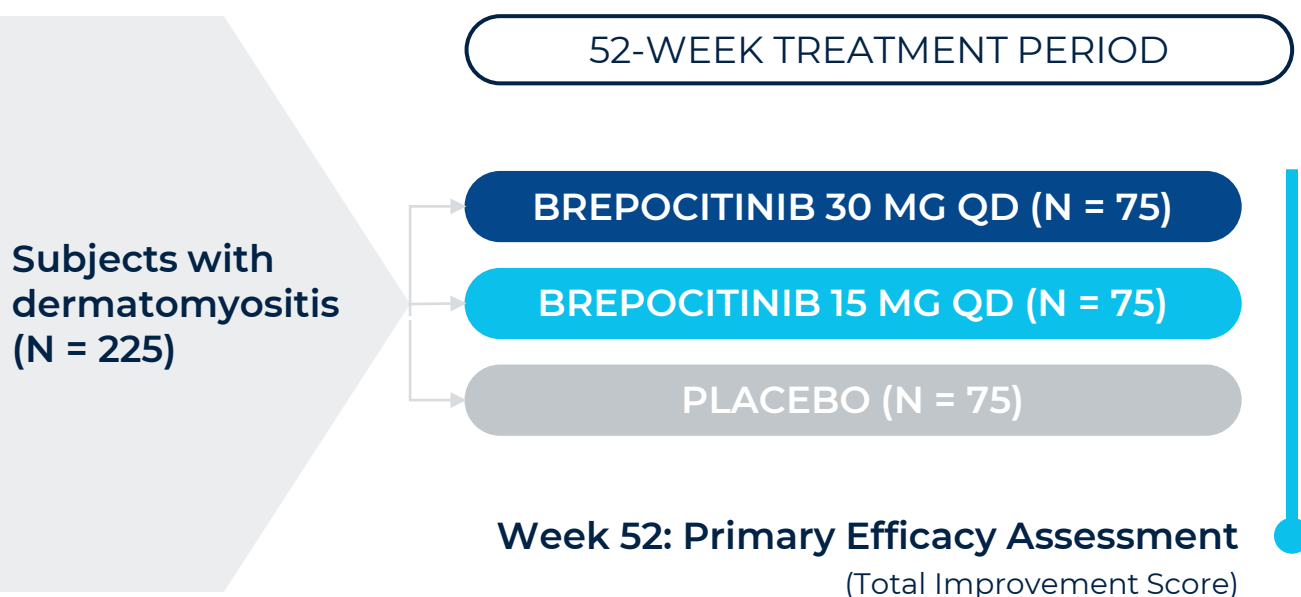
**Clinical PoC further validated by extensive JAK case report literature<sup>4</sup>**

1) Paik et al, Arth Rheum (2020)  
2) Aggarwal et al, NEJM (2022)  
3) STIR study: median is the only statistical analysis provided; ProDERM study: mean is the only statistical analysis provided  
4) Paik et al, Clin Exp Rheum (2022)

## DERMATOMYOSITIS

# Single Phase 3 Study

Phase 3 program will use the total improvement score (TIS), a validated myositis improvement index that served as basis of approval for IVIg. Topline results expected in 2025 → potentially the next approved drug of any modality for dermatomyositis.



### 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
<b>Global Development Programs</b>			
<b>Brepocitinib</b> Dual TYK2/JAK1 inhibitor		Oral, once-daily	Phase 3
<b>OCTAGAM 10%</b> Human immunoglobulin (IVIg)		IV Infusion	Approved
<b>IgPro20</b> Human immunoglobulin		Subcutaneous infusion	Phase 3
<b>Dazukibart</b> Anti-IFN- $\beta$ mAb		IV infusion	Phase 3 <sup>1</sup>
<b>Efgartigimod</b> Anti-FcRn antibody fragment		Subcutaneous injection	Phase 2/3 <sup>2</sup>
<b>ULTOMIRIS (ravulizumab)</b> Anti-C5 mAb		IV Infusion	Phase 2/3
<b>Ex-US Development Programs</b>			
<b>OLUMIANT (baricitinib)</b> JAK1/2 inhibitor	Investigator-Initiated	Oral, once-daily	Phase 3 <sup>3</sup> – France only

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

1) Basket study in PM & DM.

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

3) N = 62 patients

CONFIDENTIAL



# 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 States<sup>1</sup>

### Key Symptoms

Nodule, abscess, and tunnel formation in skin folds

### Comorbidities

Metabolic syndrome<sup>2</sup>, spondylarthritis<sup>3</sup>, inflammatory bowel disease<sup>4</sup>

>2x

Increased suicide risk for patients living with HS compared to the general population<sup>5</sup>

1) Estimates for moderate/severe HS only; based on Phan et al, Biomed Derm 2020  
2) Sabat et al, PLoS One (2012)  
3) Shlyankevich et al, J Am Acad Derm (2014)  
4) Deckers et al, J Am Acad Derm (2017)

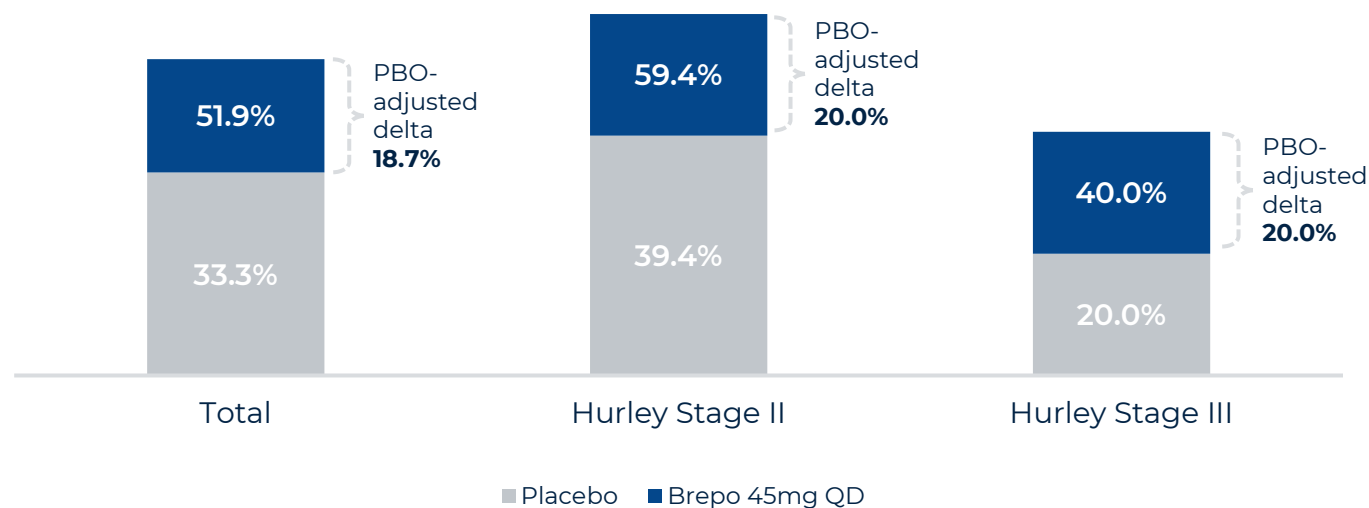
5) Thorlacious et al, J Invest Dermatol 2018

## BREPOCITINIB IN HS

# Clinical Proof-of-Concept

In a 16-week Phase 2 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

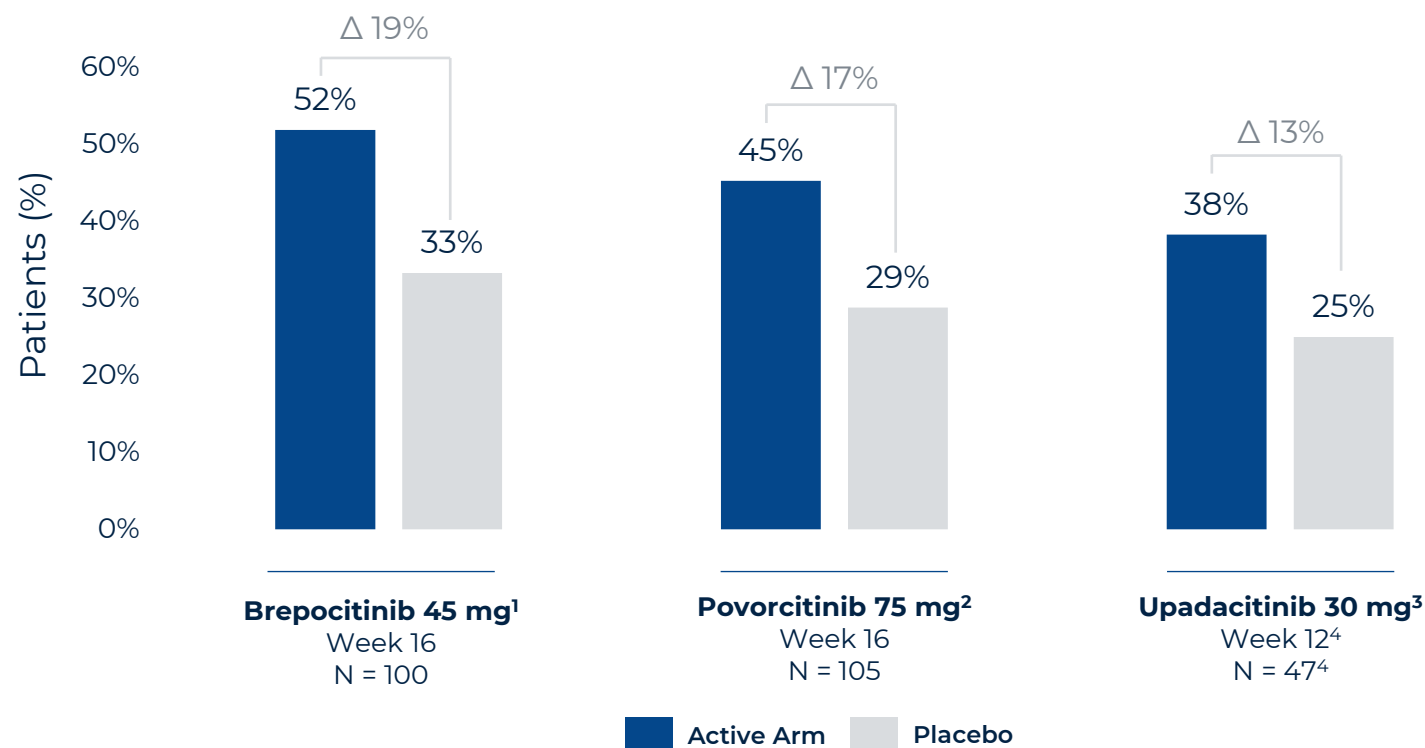
Key secondary endpoints, including total AN count and time to first flare, also achieved statistical significance

## BREPOCITINIB IN HS

# Dual TYK2/JAK1 Inhibition May Provide Greater Efficacy than Inhibition of JAK1 Alone

### HiSCR50 Response

Cross-Study Comparisons; No Head-to-Head Data Available



Absolute and placebo-adjusted results numerically better than other oral agents and comparable to leading biologics

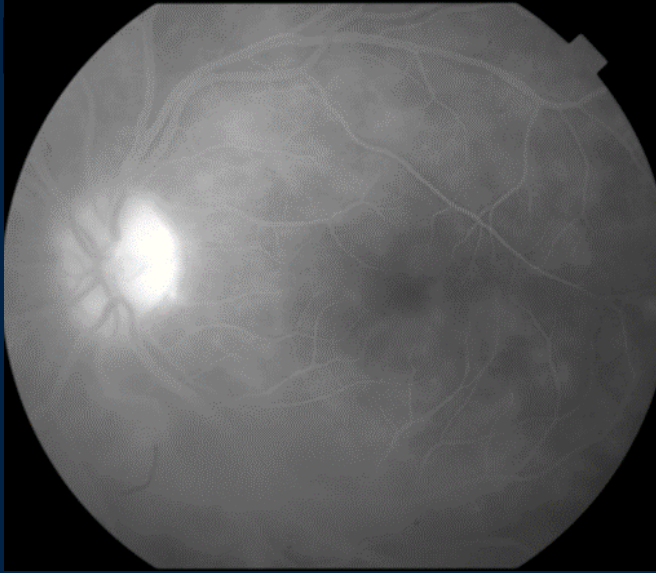
Results suggest that addition of TYK2 inhibition may contribute to better efficacy in HS; inhibition of Th17 (IL-23) axis in HS extensively validated by IL-17-targeting biologics (eg Cosentyx)

1) Kimball et al, EADV 2022

2) Kirby et al, EADV 2022 Poster P0004

3) Kimball et al, AAD 2023 Poster 43799

4) Primary endpoint of upadacitinib Phase 2 study was HiSCR at 12 weeks. N represents active arm only as primary statistical analyses were performed in reference to prespecified historical placebo control (N = 259). Active arm performance at Week 16 for UPA30 was 40%.



#### 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 75,000<sup>1</sup> people in the United States

**30,000**

New cases of legal blindness attributable to NIU in the US each year<sup>1</sup>

### Most Common Symptoms

Light sensitivity, pain, redness and floaters

### Etiology

Idiopathic, or secondary to systemic autoimmune diseases<sup>2</sup>

**1**

Approved targeted therapy (Humira)

1) Thorne et al, JAMA Ophthalmol. (2016)  
2) De Smet et al, Prog in Ret and Eye Res (2011)

ONGOING

## Phase 2 Study in NIU

Two dose-arm study designed to provide rapid validation of TYK2/JAK1 approach in NIU. Enrollment now complete; topline data expected in Q1 2024

Subjects  
with active,  
non-anterior NIU  
(N = 24)



BREPOCITINIB 45 MG QD (N = 16)

BREPOCITINIB 15 MG QD (N = 8)

Week 24  
Primary Efficacy Assessment  
(Treatment Failure)

### Eligible Patients

Adult subjects with active intermediate, posterior, or panuveitis

### Primary Endpoint

Proportion of subjects meeting treatment failure criteria on or after Week 6 up to Week 24

**Predefined success criterion:** 45 mg treatment failure rate of no greater than 70%\*

### Other Endpoints

- Treatment failure rate at Week 52
- Change in best corrected visual acuity

\* Assumed synthetic placebo rate of 80-90%; based on historical placebo rates, adjusted for more aggressive mandatory corticosteroid taper in brepocitinib study





## APPENDIX 1

# Additional References

### Slide 6: Safety Overview

#### TEAEs Incidence Rate Chart

Brepocitinib source data: Brepocitinib Clinical Study Reports (Priovent 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 ICxx (% 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; Priovent 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: Priovent 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)