# Introduction to Priovant

April 2024

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# 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:** Clinically meaningful results in seven phase 2 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

**Two Registrational Programs:**

Single registrational Phase 3 study in dermatomyositis (DM) nearly fully enrolled with data expected in 2025; potential NDA submission by YE 2025

Phase 3 program in non-infectious uveitis expected to initiate in 2H 2024

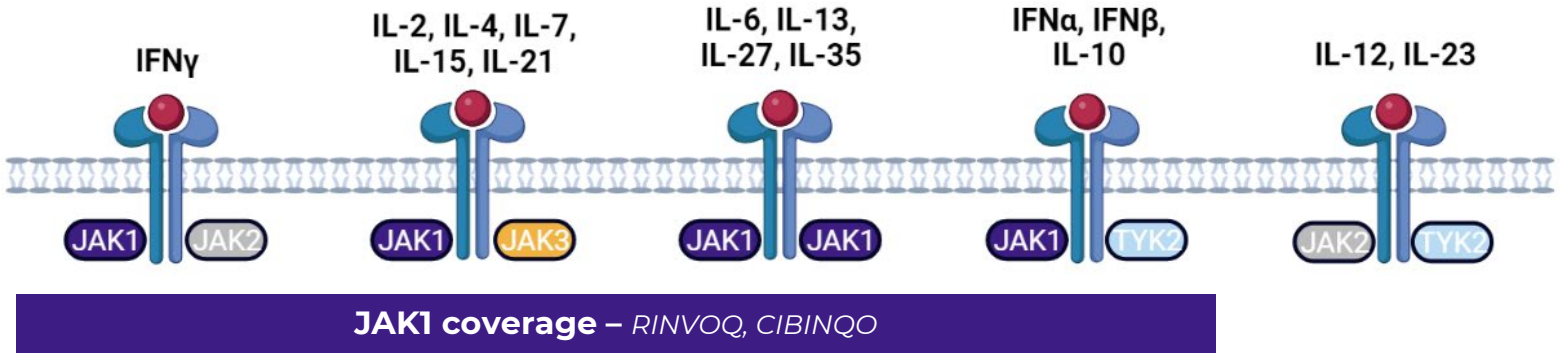
ORAL BREPOCITINIB

# 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)



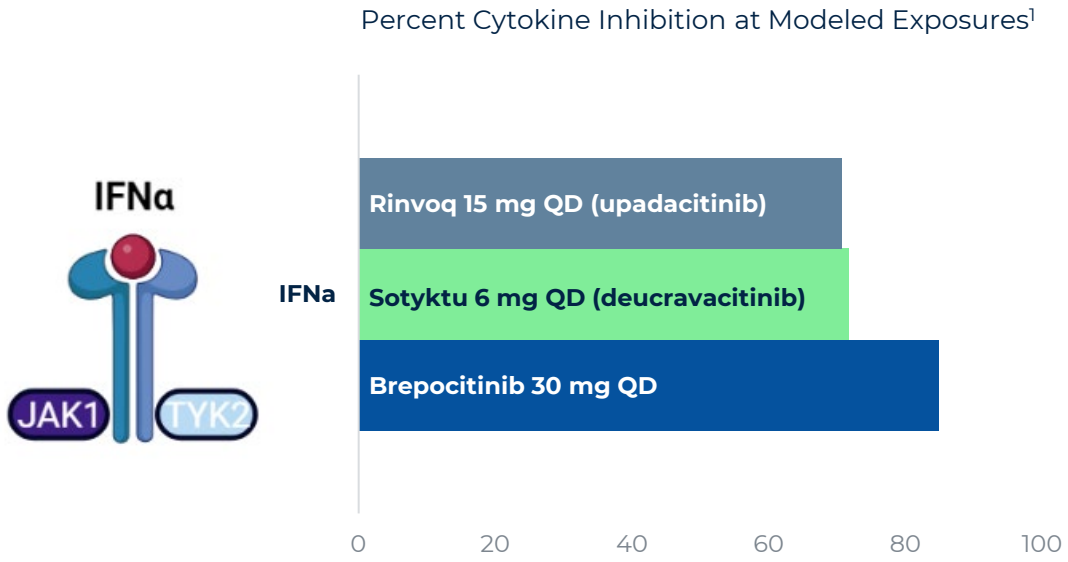

Brepocitinib was designed to target both TYK2 and JAK1

**Greater coverage vs. TYK2s** | **Dual Hit** | **Greater coverage vs. JAK1s**

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

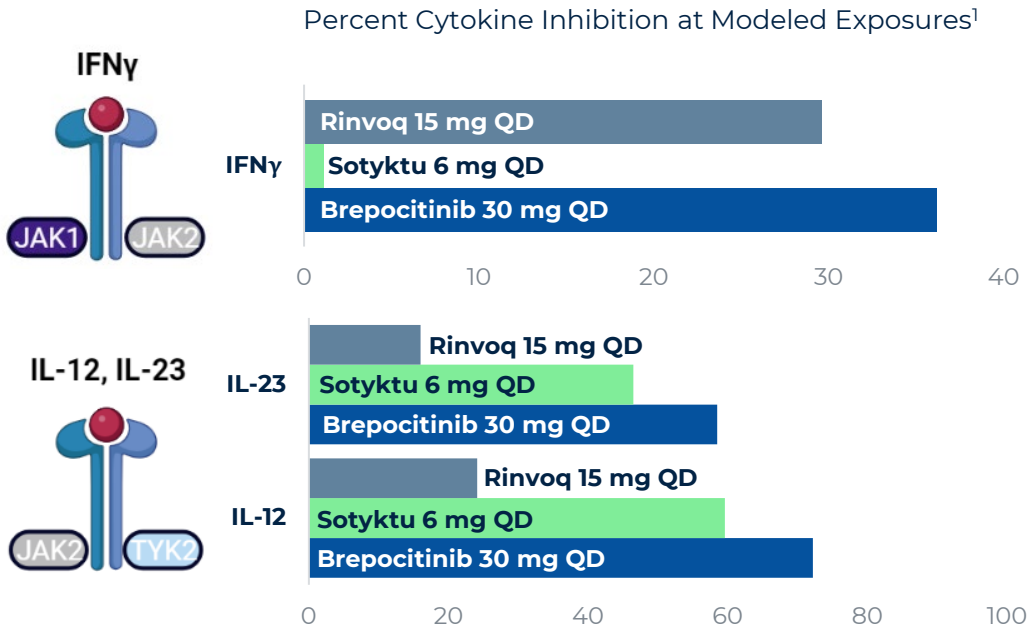
# In Vitro Data Support Mechanistic Benefits of Dual Inhibition of TYK2 and JAK1

## Dual Hit




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

## Greater Coverage




Brepocitinib may recapitulate <u>in a single molecule</u> 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

# Clinically Meaningful Results in Seven Completed Phase 2 Studies

| Study Population | N[1] | Brepocitinib Dose | Primary Endpoint Result | |
|---|---|---|---|---|
| **Psoriatic Arthritis**<br>Patients with active PsA | 218 | 30 mg once daily | 23.4% placebo-adjusted<br>ACR20 RR at week 16 | **P = 0.0197** |
| **Plaque Psoriasis**<br>Patients with moderate-to-severe PsO | 212 | 30 mg once daily | -10.1 placebo-adjusted<br>CFB in PASI Score at week 12 | **P < 0.0001** |
| **Ulcerative Colitis**<br>Patients with moderate-to-severe UC | 167 | 30 mg once daily | -2.28 placebo-adjusted<br>CFB in Mayo Score at week 8 | **P = 0.0005** |
| **Alopecia Areata**<br>Patients with moderate-to-severe AA | 94[2] | 30 mg once daily[3] | 49.18 placebo-adjusted<br>CFB in SALT Score at week 24 | **P < 0.0001[4]** |
| **Hidradenitis Suppurativa**<br>Patients with moderate-to-severe HS | 100 | 45 mg once daily[5] | 18.7% placebo-adjusted<br>HiSCR Rate at week 16 | **P = 0.0298[4]** |
| **Crohn's Disease**<br>Patients with moderate-to-severe CD | 151 | 60 mg once daily[6] | 21.4% placebo-adjusted<br>SES-CD 50 Rate at week 12 | **P = 0.0012[4]** |
| **Non-Infectious Uveitis**<br>Patients with active, non-anterior NIU | 26 | 45 mg once daily | 29.4% Treatment Failure Rate at week 24[7] | |

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
7) Study did not include a placebo arm

CFB: change from baseline; RR: response rate; NC: not calculated

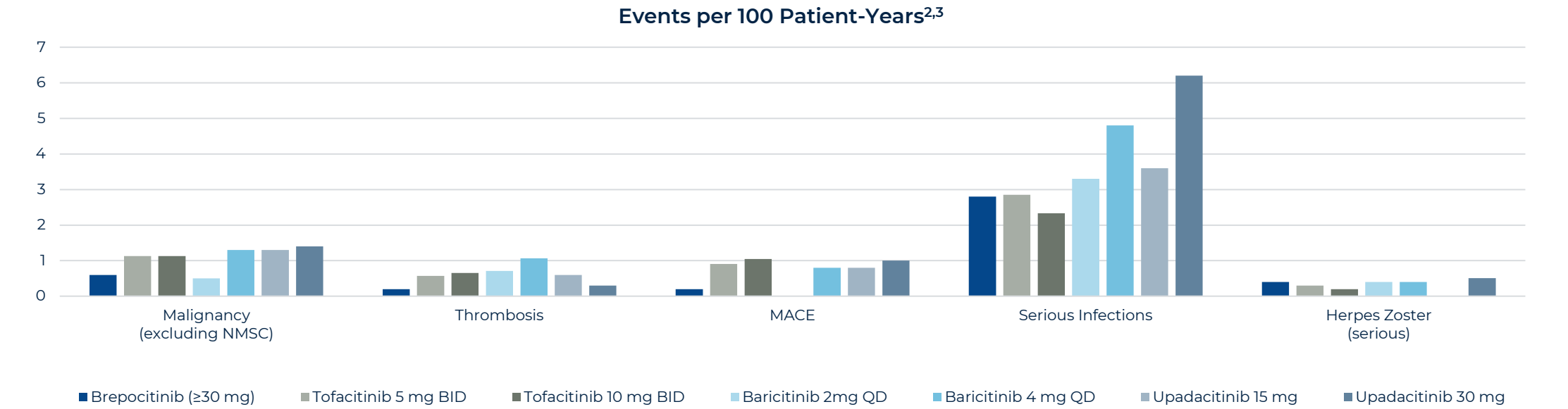
## ORAL BREPOCITINIB

# Safety Overview

Clinical experience in more than 1,400[1] exposed subjects and patients suggests a safety profile consistent with those of approved JAK inhibitors

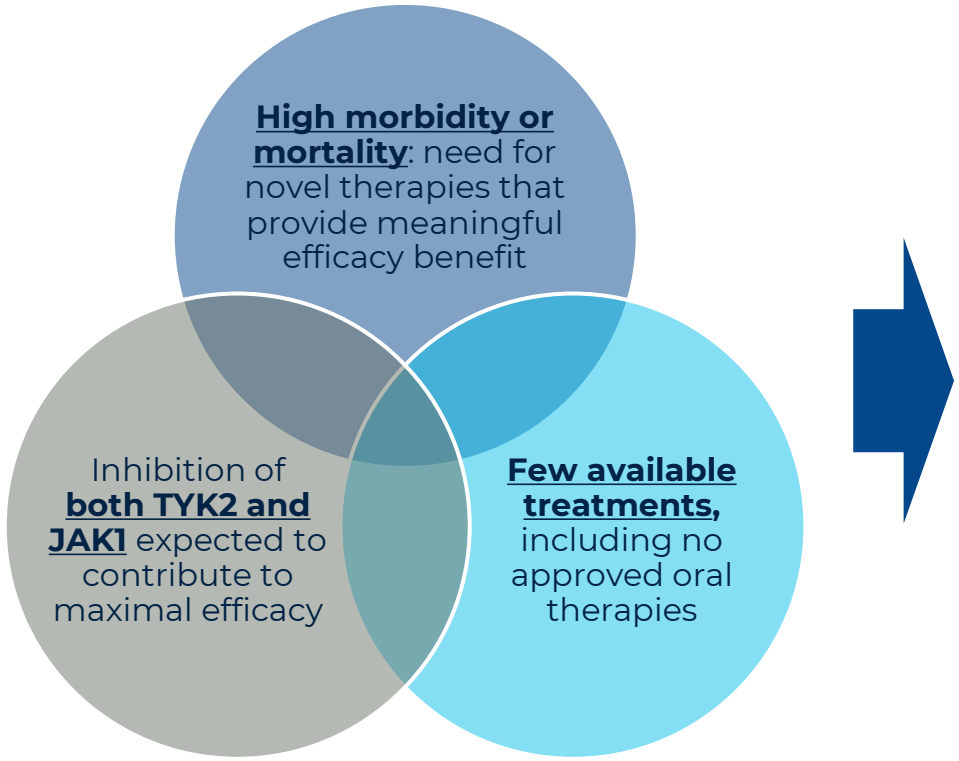
### Comparable Incidence Rates of TEAEs of Interest vs. Approved JAKs

*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 7 completed Phase 2 studies (PsA, PsO, AA, UC, Vitiligo, HS, SLE) in addition to 1 ongoing Phase 2 study (Crohn's).
2) Analysis includes only completed studies for which CSRs are available (all completed Phase 2 studies listed above). 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 and Planned Registrational Programs

| | |
|---|---|
| **Dermatomyositis** | • Large orphan indication with no NCEs approved in past 60 years<br>• Registrational phase 3 study ongoing – TLR expected in 2025 |
| **Non-Infectious Uveitis** | • Positive topline data from phase 2 study represents the best Treatment Failure rates observed to date among active NIU studies measuring this registrational endpoint<br>• Initiation of phase 3 program expected 2H 2024 |

## Potential Expansion Opportunities

| | |
|---|---|
| **JAK1- and TYK2-mediated indications** | • Ongoing evaluation of other high morbidity specialty and orphan diseases for which dual inhibition of JAK1 and TYK2 is expected to provide differentiated benefit |

# Dermatomyositis

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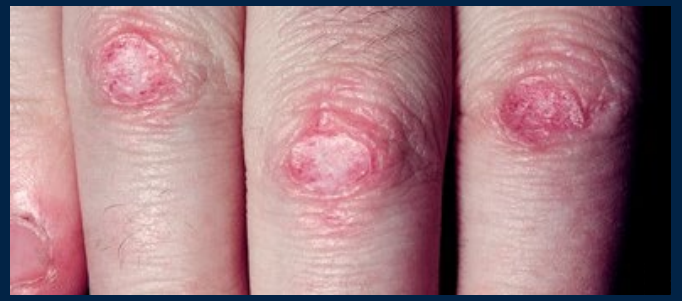
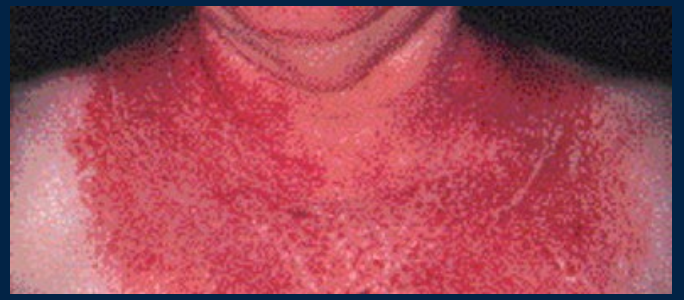


**GOTTRON'S PAPULES**

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[1] adults in the United States

**10-40%** Mortality at five years[2]

**100%** Red, painful, itchy skin rash often disseminated across substantial body surface area

**88%** Have proximal muscle weakness[3], limiting activities of daily living (ADL)

- 63% struggle to climb stairs[4]
- 50% report falls[5]
- 33% require mobility aids[5]

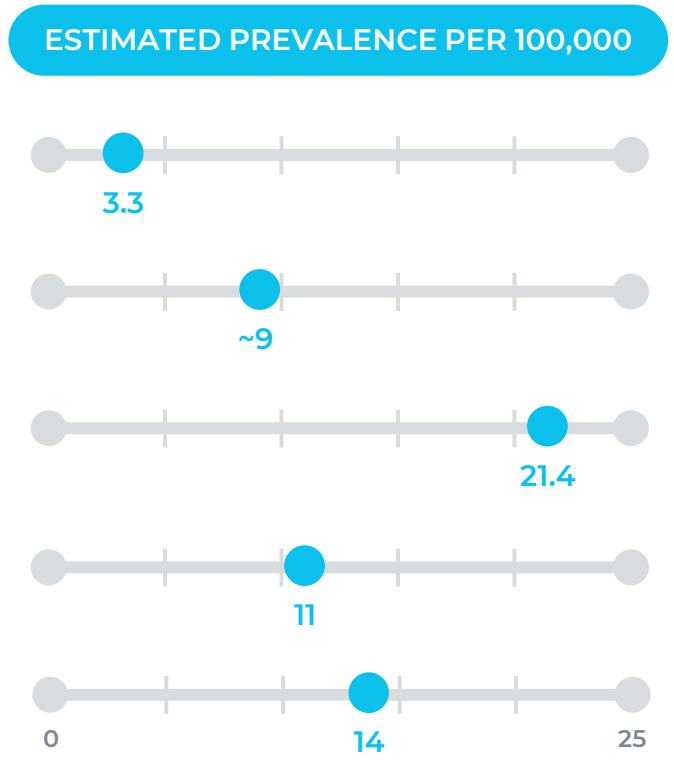
**0** Other oral therapies in industry-sponsored late-stage development[5]

**0** NCEs approved in last 60 years

1) PriovantTx 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) Priovant/TMA Survey (data on file)
5) MSU Burden of Disease Survey 2022
6) 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

**Foch et al** (2024)
Analysis of MarketScan database from 2018-2021

**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

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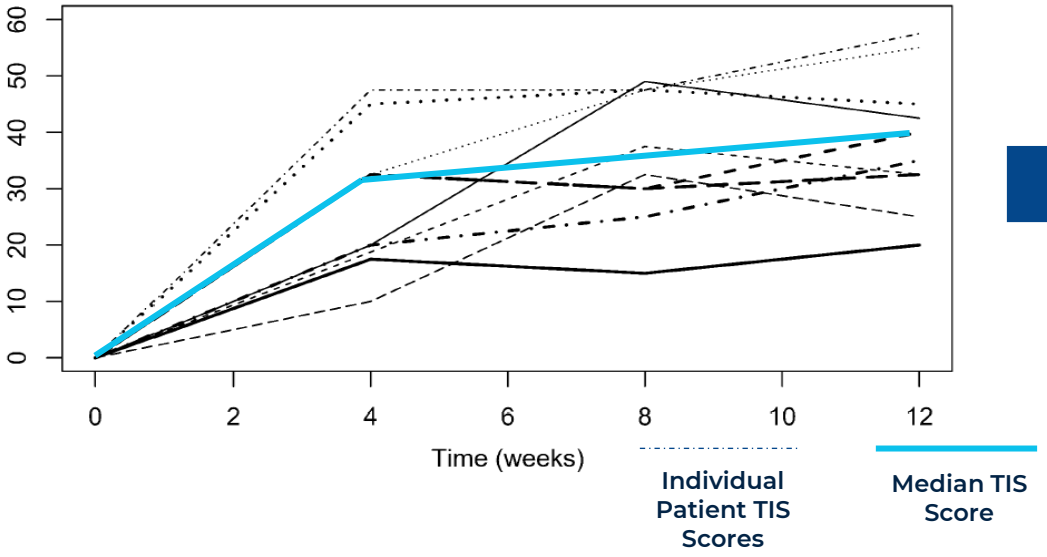
## JAK INHIBITION IN DERMATOMYOSITIS

# 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

**Study of Tofacitinib in Refractory Dermatomyositis (STIR)[1]**
**Total Improvement Scores**




**STIR Study**
TIS Outcomes

***Open-label, single-arm***

**100%**
TIS20 Response Rate at Week 12

**40**
Median TIS Score at Week 12[3]

**ProDERM Phase 3 Study (IVIg)[2]**
TIS Outcomes

***Double-blind, placebo-controlled***

**79%**
TIS20 Response Rate at Week 16

**43**
Mean TIS Score at Week 12[3]

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

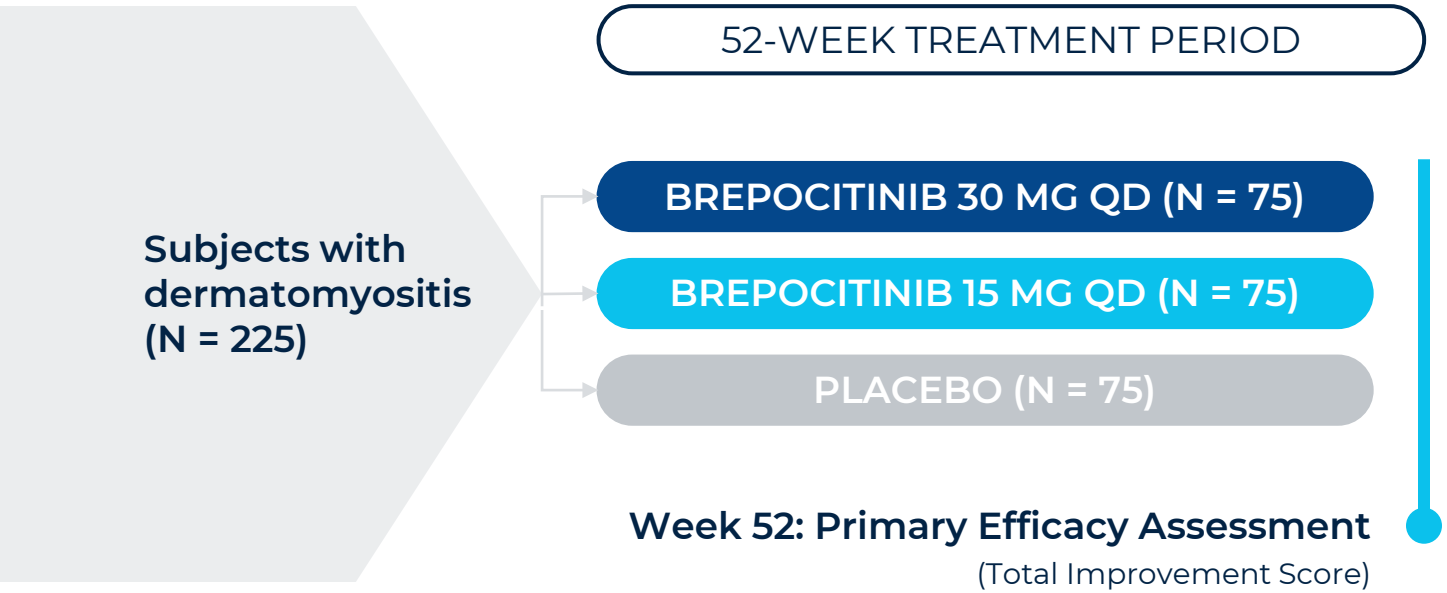
**Clinical PoC further validated by extensive JAK case report literature[4]**

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 ≥ 40 points
- CFB in HAQ Disability Index Score
- CFB in CDASI Activity Score
- Reduction in prednisone dose

## Safety Endpoints

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

CFB: Change from baseline
HAQ: Health Assessment Questionnaire
CDASI: Cutaneous Dermatomyositis Area and Severity Index

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# 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 | priovant | Oral, once-daily | Phase 3 |
| **OCTAGAM 10%** Human immunoglobulin (IVIg) | octapharma | IV Infusion | Approved |
| **IgPro20** Human immunoglobulin | CSL Behring | Subcutaneous infusion | Phase 3 |
| **Dazukibart** Anti-IFN-β mAb | Pfizer | IV infusion | Phase 3[1] |
| **Efgartigimod** Anti-FcRn antibody fragment | argenx | Subcutaneous injection | Phase 2/3[2] |

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).

# Non-Infectious Uveitis

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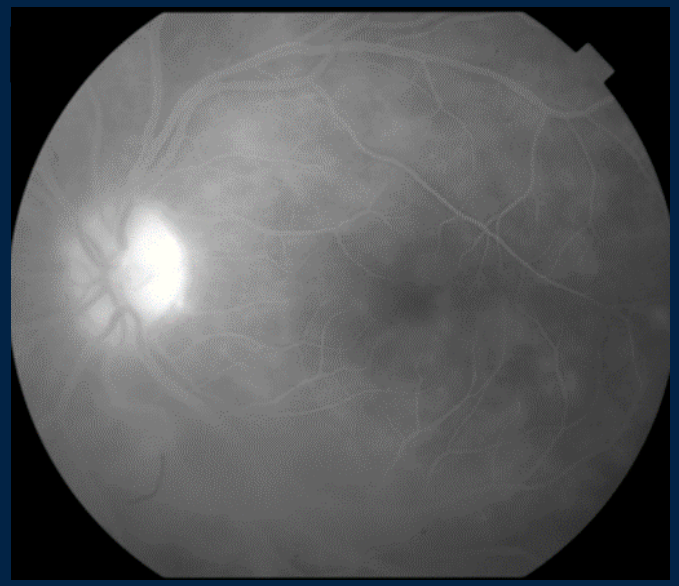


POSTERIOR SEGMENT INFLAMMATION

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 70-100,000[1] people in the United States

| | |
|---|---|
| **4th** | Leading cause of blindness among working-age population in the developed world[2] |
| **30,000** | Patients receiving biologics for non-anterior NIU, including Humira (only approved nonsteroidal therapy) and off-label medicines[3] |
| **Most Common Symptoms** | Light sensitivity, pain, redness and floaters |
| **Etiology** | Approximately half idiopathic, half in context of other systemic autoimmune disease[4] |
| **1** | Approved targeted therapy (Humira) |

1) Thorne et al, JAMA Ophthalmol. (2016)
2) Barisani-Asenbauer, T., Maca, S.M., Mejdoubi, L. et al, Orphanet J Rare Dis (2012)
3) Roivant/Priovant analysis of medical claims from Inovalon, including idiopathic and systemic disease-associated NIU.
4) Lopalco et al, Clin Exp Rheum 2018.

# Mechanistic Rationale For Brepocitinib In NIU

Dual TYK2/JAK1 inhibitor distinctively suppresses IL6, IFNy, IL12, IL23 with single targeted agent, addressing TH1- and TH17-driven autoimmunity

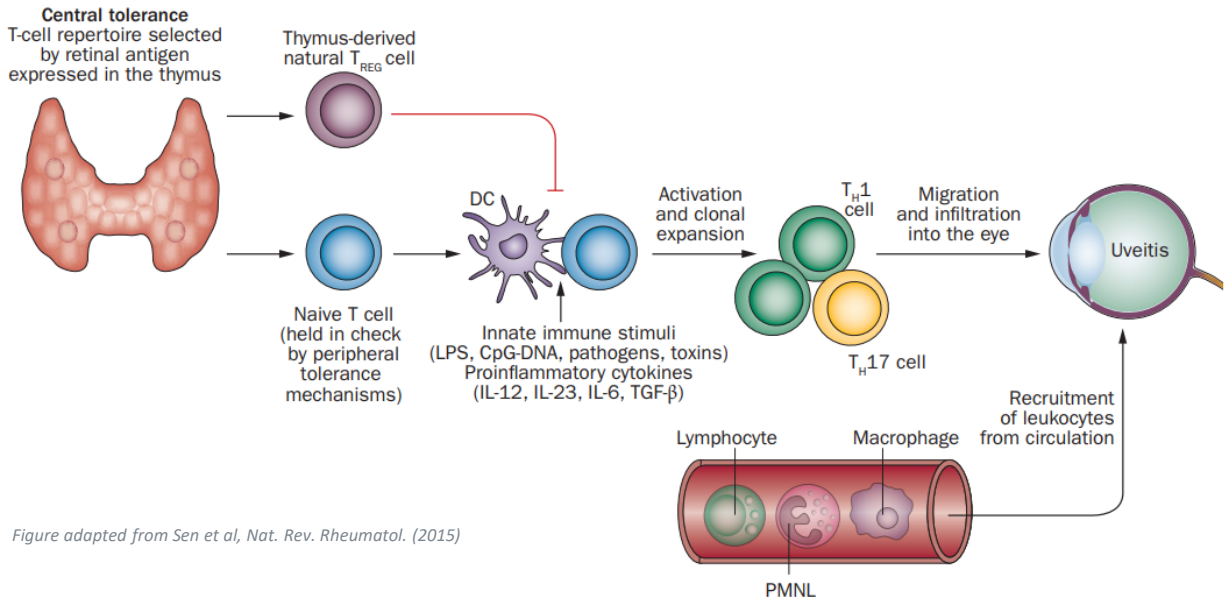



*Figure adapted from Sen et al, Nat. Rev. Rheumatol. (2015)*

***Th1 and Th17 cells are the primary pathogenic effectors contributing to the development and maintenance of uveitis***

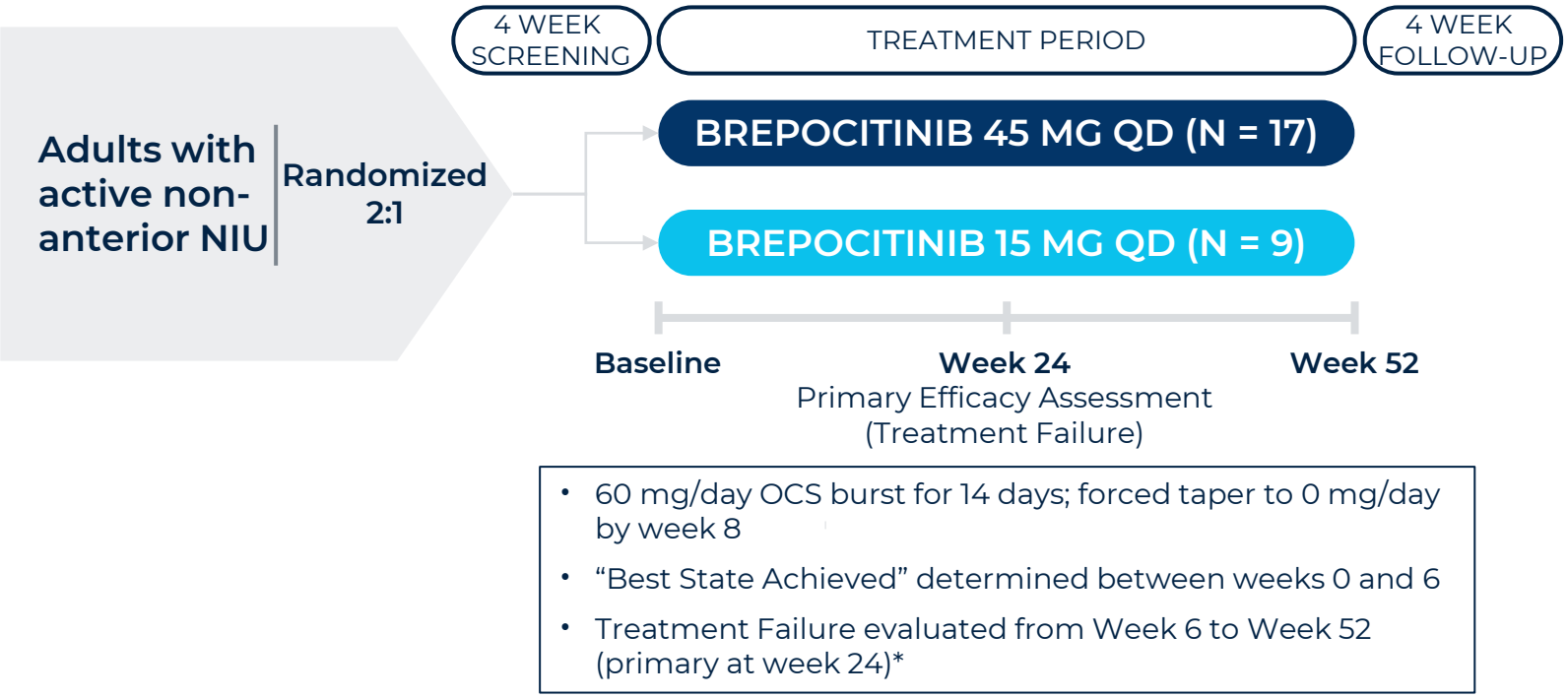
**<u>Brepo suppression of TH17 pathway</u>**
- IL6 (signalling suppressed by JAK1)
- IL23 (signalling suppressed by TYK2)

**<u>Brepo suppression of TH1 pathway</u>**
- IL12 (signalling suppressed by TYK2)
- IFNy (signalling suppressed by JAK1)

BREPOCITINIB IN NIU

# NEPTUNE Study Design

A Phase 2 Randomized, Double-Masked, Dose-Ranging Study to Investigate the Safety and Efficacy of Oral Brepocitinib in Adults with Active Non-Infectious Intermediate-, Posterior-, and Panuveitis




- 60 mg/day OCS burst for 14 days; forced taper to 0 mg/day by week 8
- "Best State Achieved" determined between weeks 0 and 6
- Treatment Failure evaluated from Week 6 to Week 52 (primary at week 24)*

## Key Efficacy Endpoints

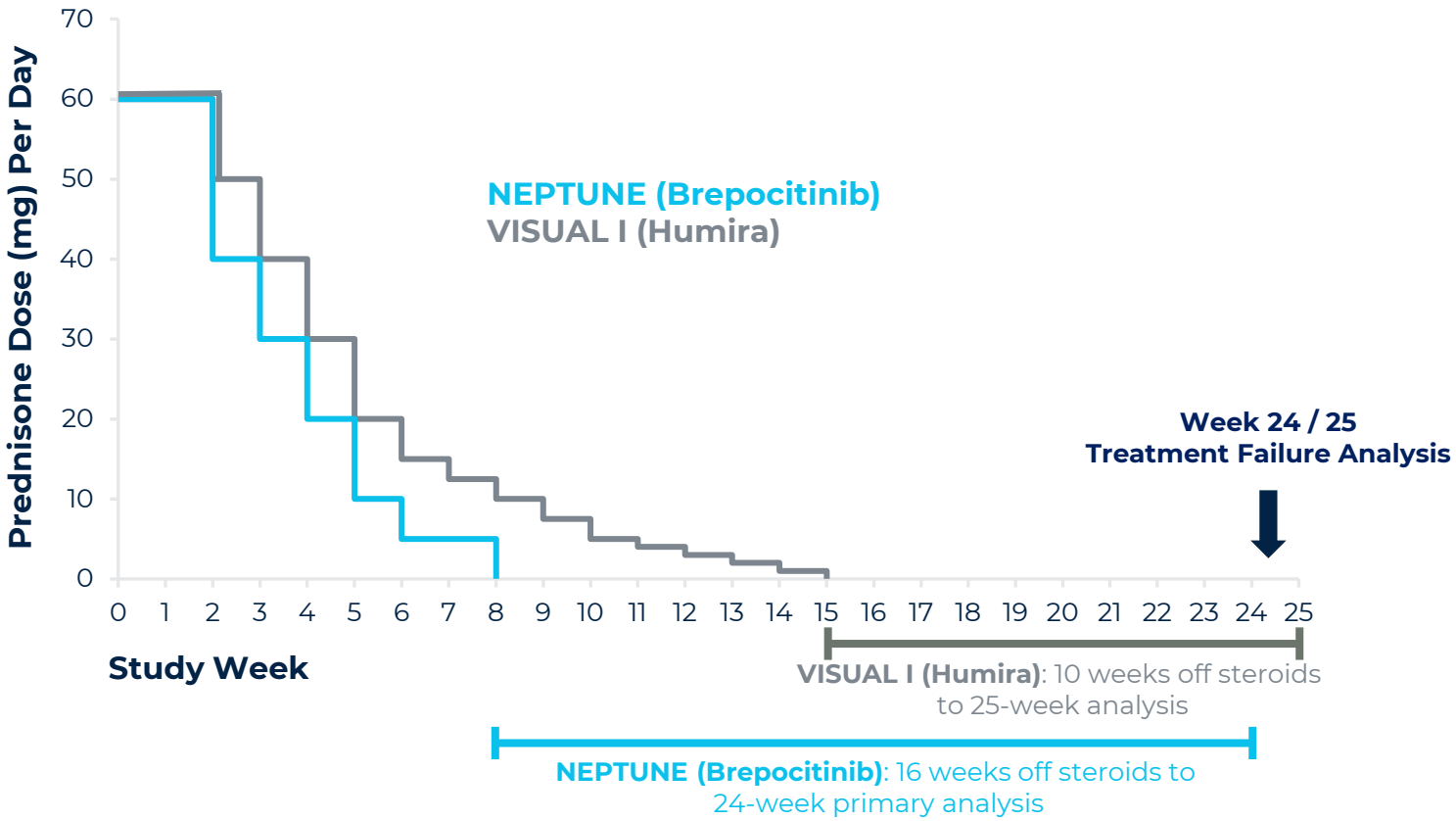
- Treatment Failure rate at Week 24 (primary)
- Treatment Failure Sub-Components: Change on ACC grade, VH grade, inflammatory lesions, and BCVA*
- Change in central subfield thickness (including macular edema)

*ACC: anterior chamber cell; BCVA: best-corrected visual acuity; IST: immunosuppressive therapy; VH: vitreous haze

BREPOCITINIB IN NIU

# Steroid Taper Sets Higher Bar Compared To Precedent Studies

NEPTUNE (brepocitinib) study is modeled on VISUAL I (active uveitis registrational study for Humira) with one key exception – brepocitinib steroid taper was more than twice as fast




## Key Implications of Different Tapers

Brepocitinib patients tapered from 60 mg/day to 0 mg/day more than twice as quickly as Humira/placebo patients in VISUAL I (6 weeks compared to 13 weeks) → ***much higher risk of flares***

- **Requires that brepocitinib act more quickly**
- **Requires brepocitinib meet higher efficacy bar to prevent flares**

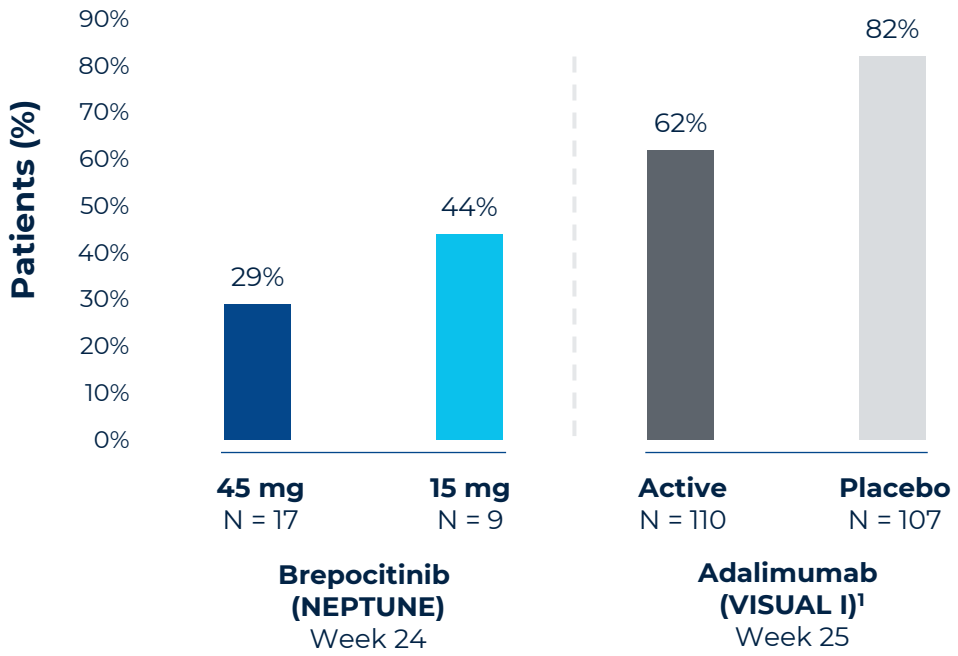
Brepocitinib had to provide steroid-free benefit for >50% longer to prevent treatment failure by week 24

- **Requires that brepocitinib demonstrate more durable steroid-sparing benefit**

## PRIMARY EFFICACY ENDPOINT INCLUDING CROSS-STUDY COMPARISON TO VISUAL I (HUMIRA)

# Treatment Failure Rate at Week 24

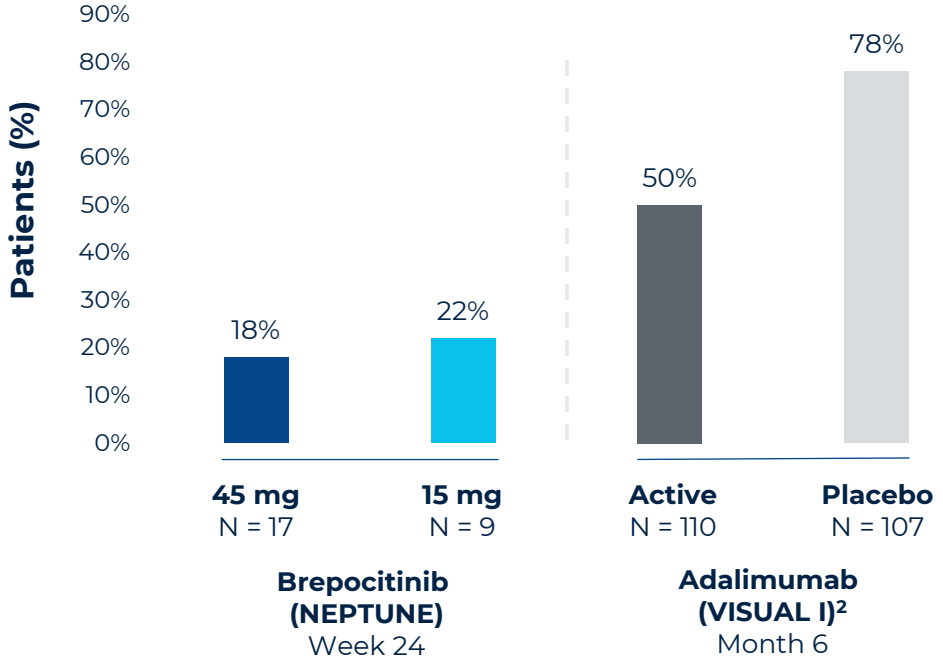
**Treatment Failure**
(ITT; ICEs Imputed as Treatment Failure)




**Brepocitinib Treatment Failure Rate Analysis:**

$$\frac{\text{Treatment Failures + Discontinuations/ICEs}^{3}}{\text{Subjects Randomized}}$$

**Treatment Failure**
(DCs Censored)




**Brepocitinib Treatment Failure Rate Analysis:**

$$\frac{\text{Treatment Failures}}{\text{Subjects Randomized}}$$

*Disclaimer: Figures reflect cross-trial comparison and not results from a head-to-head study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.*

1) Jaffe et al, NEJM (2016)
2) Data as reported on HumiraPro.com/Uveitis; DCs are censored. Analysis population for Humira unknown.
3) Intercurrent Event (ICE) = Treatment discontinuation or use of rescue medication prior to Week 24.

# Brepocitinib Proof-of-Concept in Potentially Resolving and Preventing Macular Edema

Data suggests potential to resolve macular edema and potential to prevent or reverse swelling before threshold for macular edema is reached and patient is formally diagnosed with UME

| In the 45 mg arm, at Baseline: | In the 45 mg arm, by Wk 24: | By comparison: |
|---|---|---|
| **10 patients** did *not* have macular edema (CST < 300 µm[1]) | **0 patients** *developed* macular edema **(0% occurrence rate)** | In the VISUAL I study, among patients who did not have macular edema at baseline, **50% of placebo patients developed macular edema after 6.2 months**[1]<br>• 50% of Humira patients developed macular edema after 11.1 months[2] |
| **7 patients** had macular edema (CST ≥ 300 µm) | **3 of 7 patients** had *resolution* of macular edema **(43% resolution rate)** | In a different study of patients with uveitic macular edema at baseline, **Humira resolution rates at Month 6 were 22%**[3] |

*Disclaimer: Figures reflect cross-trial comparison and not results from a head-to-head study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.*

1. CST: central subfield thickness.
2. Definition of macular edema in NEPTUNE was CST ≥ 300 µm, normalized by central reader across instrument types.
3. Jaffe et al, NEJM 2016.
4. Leclerq et al, Ophthalmology 2021.

BREPOCITINIB

# There is Limited Competition in NIU, with Few Late-Stage Treatments Currently in Development

| Molecule/Program | Sponsor | Route of Administration | Development Stage |
|---|---|---|---|
| **Global Development Programs** | | | |
| **Brepocitinib** Dual TYK2/JAK1 inhibitor | priovant | Oral, once-daily | Entering Phase 3 |
| **Humira** Anti-TNF-α mAb | abbvie | Subcutaneous injection | Approved |
| **Yutiq/Retisert** Fluocinolone corticosteroid | EyePoint Pharmaceuticals / B+L Bausch+Lomb | Intravitreal implant | Approved (Posterior NIU Only) |
| **Vamikibart** Anti-IL-6 mAb | Roche | Intravitreal injection | Phase 3 (Uveitic Macular Edema)[1] |
| **Izokibep** Small protein inhibitor of IL-17A | ACELYRIN | Subcutaneous injection | Phase 2 |
| **ESK-001** Allosteric TYK2 inhibitor | alumis | Oral | Phase 2 |

Includes ongoing and planned (announced) company-sponsored Phase 2 and 3 studies in non-anterior NIU; excludes off-label use and biosimilars, as well as terminated programs like filgotinib.
1) Uveitic macular edema comprises a subset of non-anterior NIU patients.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APPENDIX 1

# Additional References

## Slide 6: Safety Overview

**TEAEs Incidence Rate Chart**

Brepocitinib source data: Brepocitinib Clinical Study Reports (Priovant 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; Priovant 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: Priovant data on file; Chimalakonda et al, Dermatol Ther (2021); Wrobleski et al, J Med Chem (2019)

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