VYNE™ THERAPEUTICS

Corporate Presentation

July 2025

ROOTED IN INNOVATION

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Investment Highlights (NASDAQ: VYNE)

Advancing novel BET inhibitor platform to improve the lives of patients suffering from immuno-inflammatory conditions

Innovative Target & Approach

- BET inhibition represents a novel target for the treatment of immune-mediated diseases: Addressing the complex signaling of I&I diseases by disrupting inflammatory gene transcription
- Potential across broad range of immune-mediated diseases representing multi-billion-dollar opportunities

Clinical Stage Pipeline

- Repibresib (VYN201): Phase 1b PoC data in vitiligo suggest VYN201 has the potential to be category leader
- VYN202: Positive Phase 1a SAD/MAD reported; Promising unblinded Phase 1b data in moderate-to-severe PsO (n=7)
  Program supported by robust preclinical data across multiple diverse models of immune-mediated disease

Potential for Multiple Clinical Catalysts

- Repibresib (VYN201): Phase 2b trial top-line results anticipated in mid-2025
- VYN202: Preliminary PsO clinical data and promising results from multiple preclinical models support advancement of VYN202 into serious, immune-mediated diseases with limited effective treatment options

Building a Leading Early-Stage Pipeline to Address Unmet Needs in I&I Conditions

Program	Indication(s)	Route of Administration	Current Stage				Status / Next Anticipated Milestones	Rights
			Preclinical	Phase 1	Phase 2	Phase 3		
InhiBET™ Platform - Library of NCE BET Inhibitors for Any Indication Worldwide								
Repibresib (VYN201) Soft pan-BD BET inhibitor	Nonsegmental Vitiligo	Topical					• Phase 1 completed • Q2 2024: P2b initiated • Mid-2025: TLR P2b	Worldwide
VYN202 BD2-selective BET inhibitor	Serious, immune-mediated diseases with limited effective treatment options	Oral					• Q4 2024: P1a SAD/MAD Complete • July 2025: Promising preliminary P1b PsO data released; No further enrollment of study • Repeat 12-week nonclinical toxicology study	Worldwide
Ongoing evaluation for other immune-mediated and fibro-inflammatory diseases								

Based on current estimates. TLR = top-line results; SAD = Single Ascending Dose; MAD = Multiple Ascending Dose

InhiBET™ BET Inhibitor Platform

Bromodomain & Extra-Terminal Domain (BET) Inhibition for Immunology and Inflammatory Diseases

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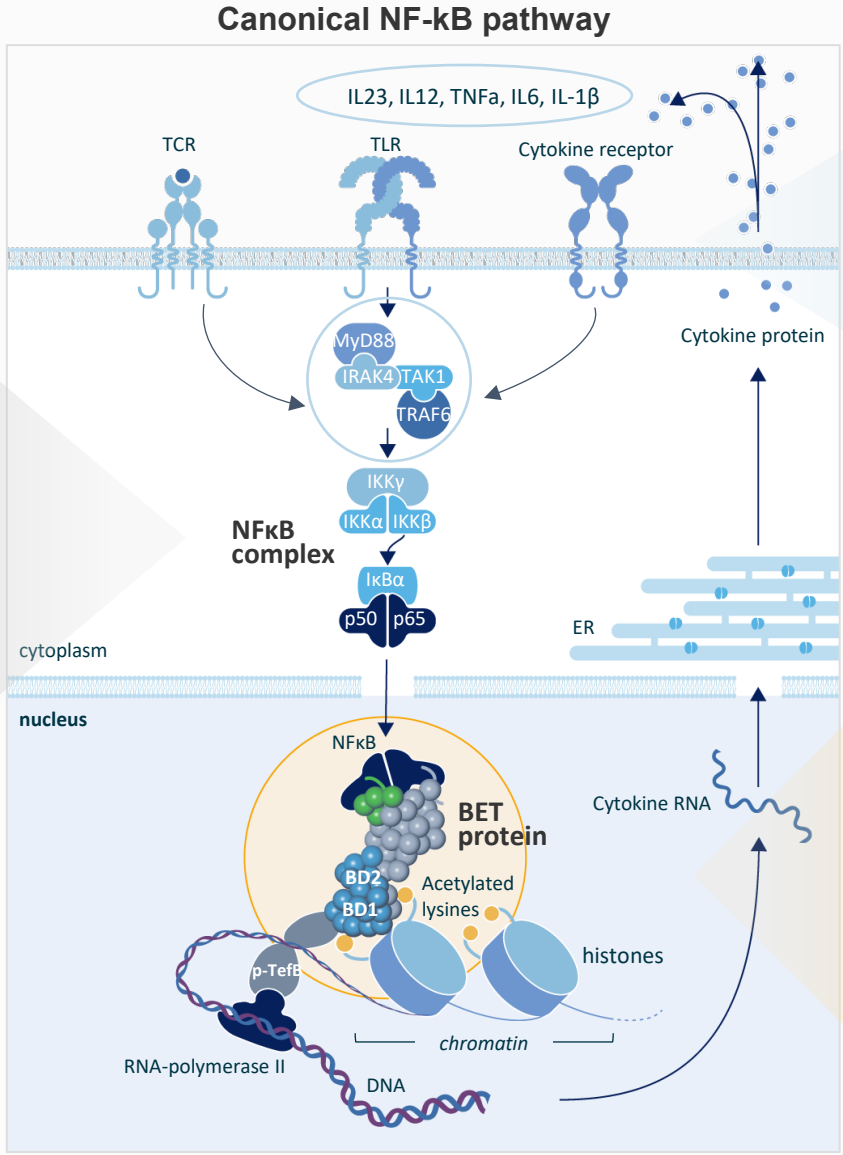
BET Proteins: Key Epigenetic Regulators of NF-kB, a Master Orchestrator of Inflammation

NF-kB Pathway

- Critical transcription factor that orchestrates production of key inflammatory cytokines and activation of multiple immune cell types.
- Significant contributor to the pathogenesis and severity of MPNs and sAML.



Validated NF-kB targets:

- Direct cytokine or receptor interaction *(e.g., IL23, IL12, TNFa, IL6, IL-1β)*
- Pre-NF-kB complex formation targets

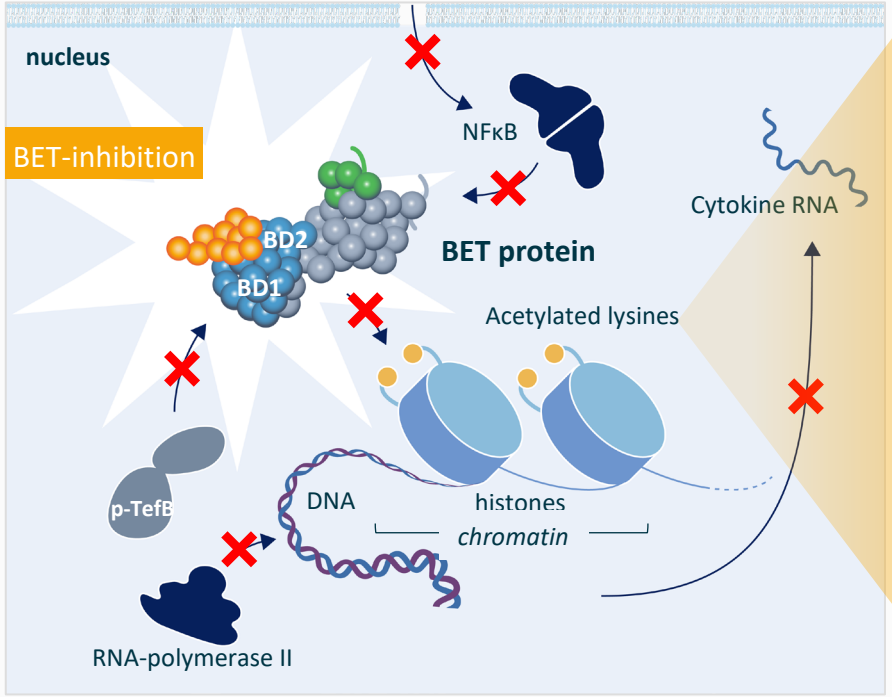
BET proteins as a NF-kB target:

- Key epigenetic enabler of NF-kB-mediated transcription, offering a novel and differentiated target
- BET inhibition is agnostic to upstream mediators (validated targets) of the NF-kB pathway, therefore is less susceptible to immunological redundancy but without having a broad immunosuppressive effect

TCR (T cell receptor) and TLR (Toll-like receptor); Adapted from Wang, N., Wu, R., Tang, D. *et al.* The BET family in immunity and disease (2021); Sullivan JY and Fleischman AG, Relating NF-kB regulation to MPN pathogenesis, Blood 143 (23):2345 (2024); Oh et al, Mass cytometry analysis reveal hyperactive NF kappa B signaling in myelofibrosis and secondary acute myeloid leukemia, Leukemia. Dec 23;31(9):1962 (2016)

BET Inhibition: A Novel Mechanism for the Treatment of I&I Conditions

BET Inhibition's Impact on Multiple Inflammatory Pathways Provides Potential to Address a Broad Range of Immune-Mediated Diseases



Primary Cell Type[1]	Th1/Tc1	Th17	Myeloid cells	B Cells
Cytokine Pathway[2]	• IL-12 • IFNγ • *BATF*	• IL-17 • IL-23 • IL-21 • *RORC*	• TNF • IL-6 • IL-1, • Chemokines • Adhesion molecules	• BAFF • IL-21 • IL-19 • IL-22
Potential Diseases[3]	• Vitiligo • Lichen Planus • Alopecia Areata • Crohn's	• PsO • PsA • HS • IBD • AxSpA	• RA • PsO • PsA • HS • IBD • AxSpA	Autoantibody-mediated diseases (e.g., SLE, RA)

Majority of immune-mediated and chronic inflammatory diseases are heterogeneous and driven by multiple immune pathways and cell types

1. Cell types involved in inflammation and autoimmunity. Th1: Helper T cell Type 1; Tc1: Cytotoxic T cell Type 1; Th17: IL-17 producing helper T cell
2. Cytokines and key mediators involved in each cell type. NF-kB is involved in both production and signaling of certain of the cytokines, e.g., TNF, IL-17. Transcription factors are in italics
3. List not exhaustive

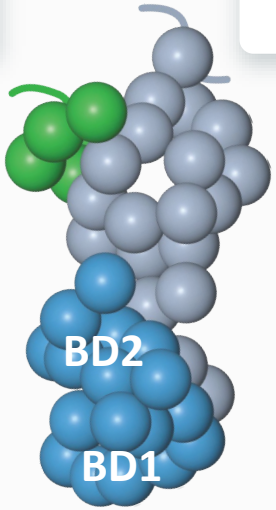
VYNE's Drug Design Strategy

Optimize benefit/risk profile of BET inhibitors to target immune-mediated diseases

Repibresib (VYN201)
Pan-BD BET Inhibitor

Maximize local effect & minimize systemic exposure

- Tissue targeted administration routes & formulations
- Soft drug / drug delivery strategies to reduce impact of BD1 inhibition on steady-state gene regulation



VYN202
BD2-Selective BET Inhibitor

Improve efficacy and tolerability through BD2-selectivity

- Class-leading BD2 vs. BD1 selectivity for systemic administration
- BD2 activity more relevant to inflammatory gene expression
- Minimize BD1 inhibition to protect against steady-state gene disruption

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Gilan et al, Science. 2020 April 24; 368(6489): 387–394
Dawson et al, Science 2020; Belkina, Nikolajczyk & Denis, J. Immunol. 2013

Repibresib (VYN201): Vitiligo

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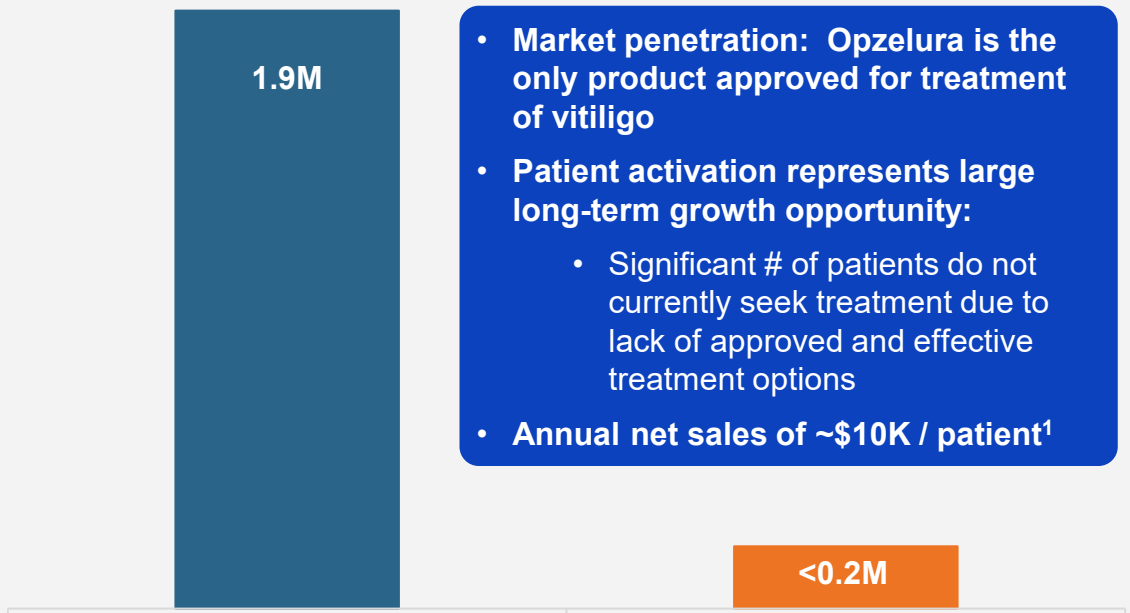
Vitiligo Represents a Large and Growing Market Opportunity

Addressable Market : a Significant Unmet Need

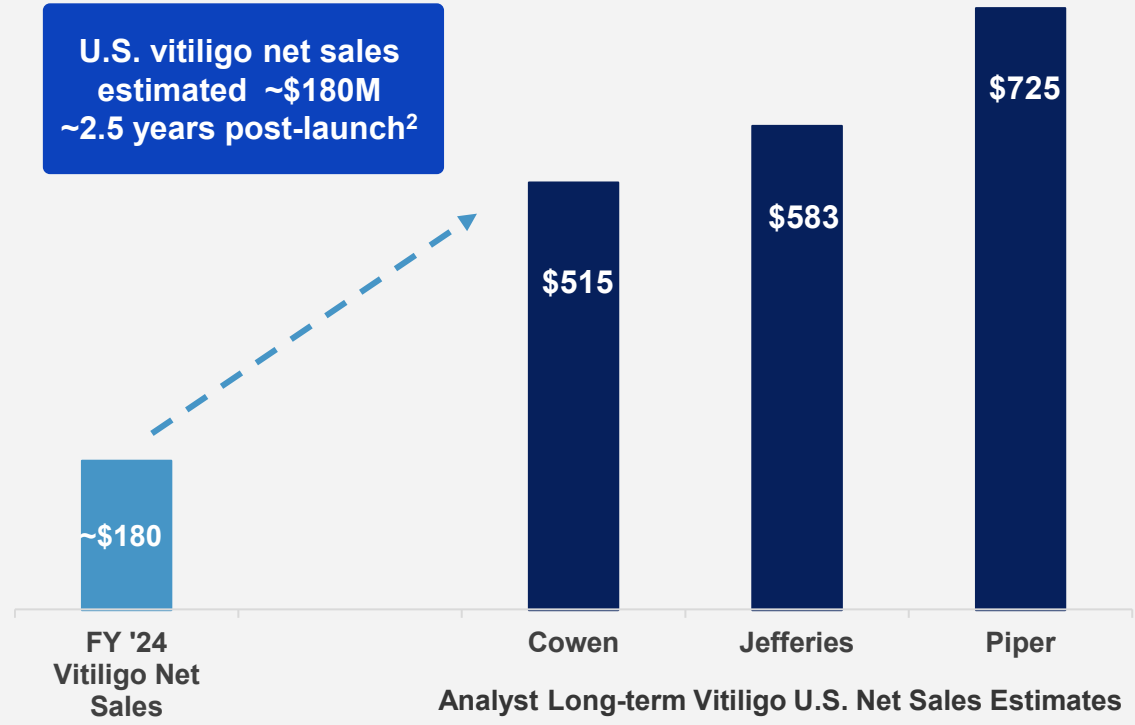


- **Market penetration: Opzelura is the only product approved for treatment of vitiligo**
- **Patient activation represents large long-term growth opportunity:**
  - Significant # of patients do not currently seek treatment due to lack of approved and effective treatment options
- **Annual net sales of ~$10K / patient[1]**

Opzelura® (ruxolitinib) cream 1.5%

$ in millions

U.S. vitiligo net sales estimated ~$180M ~2.5 years post-launch[2]



Analyst Long-term Vitiligo U.S. Net Sales Estimates

Only one drug approved, treatment is dominated by non-specific therapies including topical steroids and phototherapy

Source: Gandhi et al. JAMA Dermatol. 2022;158(1):43-50; Kruger. 2012;51(10):1206-1212; Rangu. J Clin Dermatol Ther. 2021;7:070; Pandya. AAD 2023 Presentation; Incyte Corporate Pres. Aug. 2023; TD Cowen research dated Feb. 2025 (2033 sales); Jefferies research dated Feb 2024 (2033 sales); Piper research dated Jan. 2023 (2030 sales);

1. Opzelura estimated pricing: $2k per 60g tube*10 tubes per patient per year less GTN discount of 50% per Incyte mgmt.; 2. Estimated: FY'24 U.S. net sales: $447M with vitiligo representing ~40% of TRx per Incyte mgmt.

Repibresib (VYN201): Phase 1 Proof-of-Concept

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Repibresib (VYN201): Phase 1b Study in Active Vitiligo Patients

Study Design

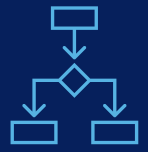
Treatment on the face and target lesion on trunk of active vitiligo patients for up to 16 weeks of QD treatment

- **N = up to 30: 3 cohorts, evaluating 0.5%, 1.0% and 2.0% strengths**
- Safety assessments include TEAEs, pharmacokinetics and local skin tolerance
- Exploratory efficacy assessments include F-VASI, biomarkers and photography

Key inclusion/exclusion criteria:

- Subjects with a clinical diagnosis of active non-segmental vitiligo. An active vitiligo lesion is defined as evidence of hypochromic areas / borders and/or confetti-like depigmentation and/or peri-lesional inflammation and/or Koebner phenomenon.
- Facial-Vitiligo Area and Severity Index Score (F-VASI) of ≥0.5.
- Two contralateral active vitiligo target lesions on non-facial anatomical areas. Non-facial target lesion areas should not include hands, wrists, feet, or elbows.
- The presence of leukotrichia should not exceed 50% of the full face or 50% of each non-facial target lesion.

Primary objectives of Phase 1b:

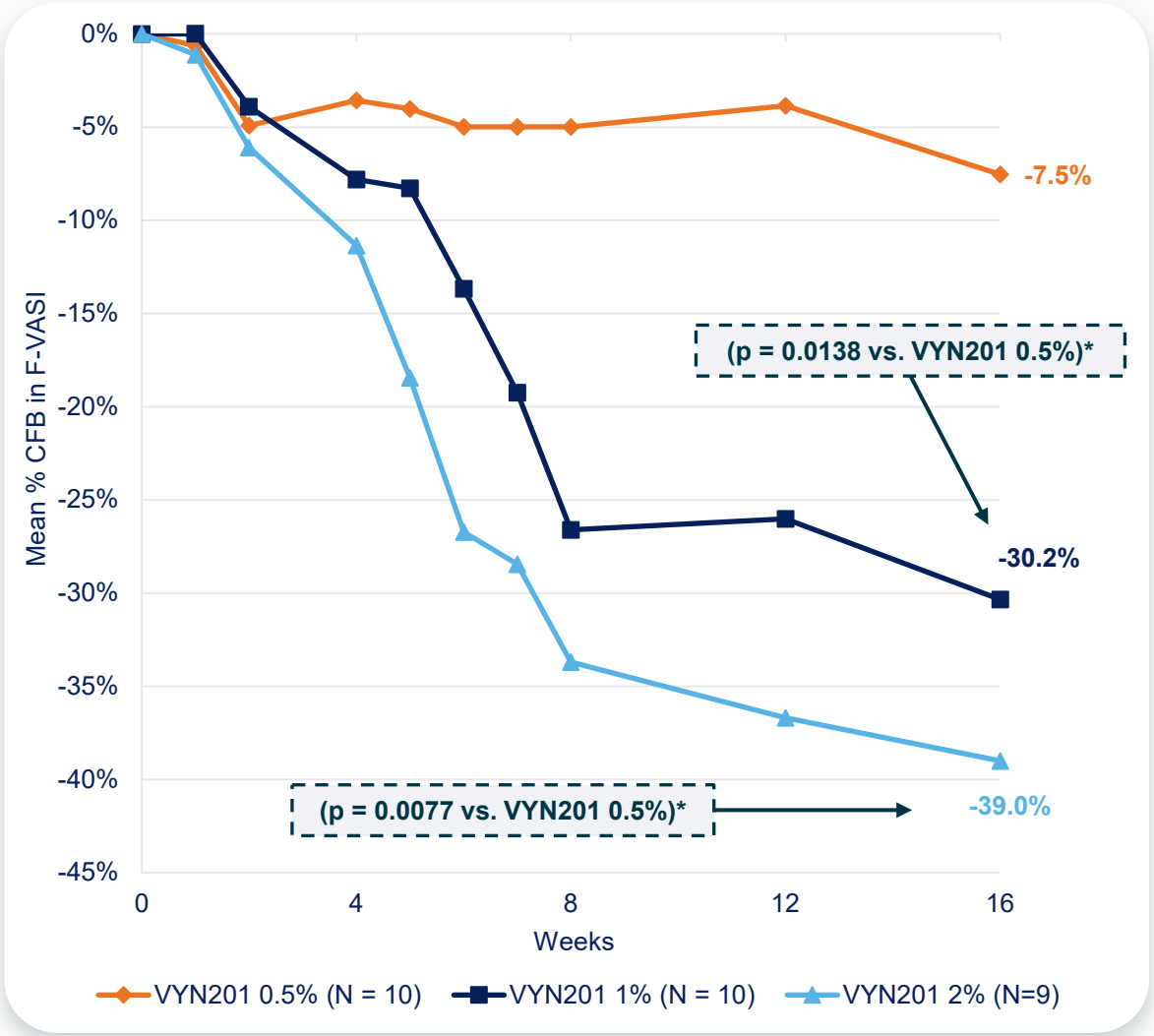


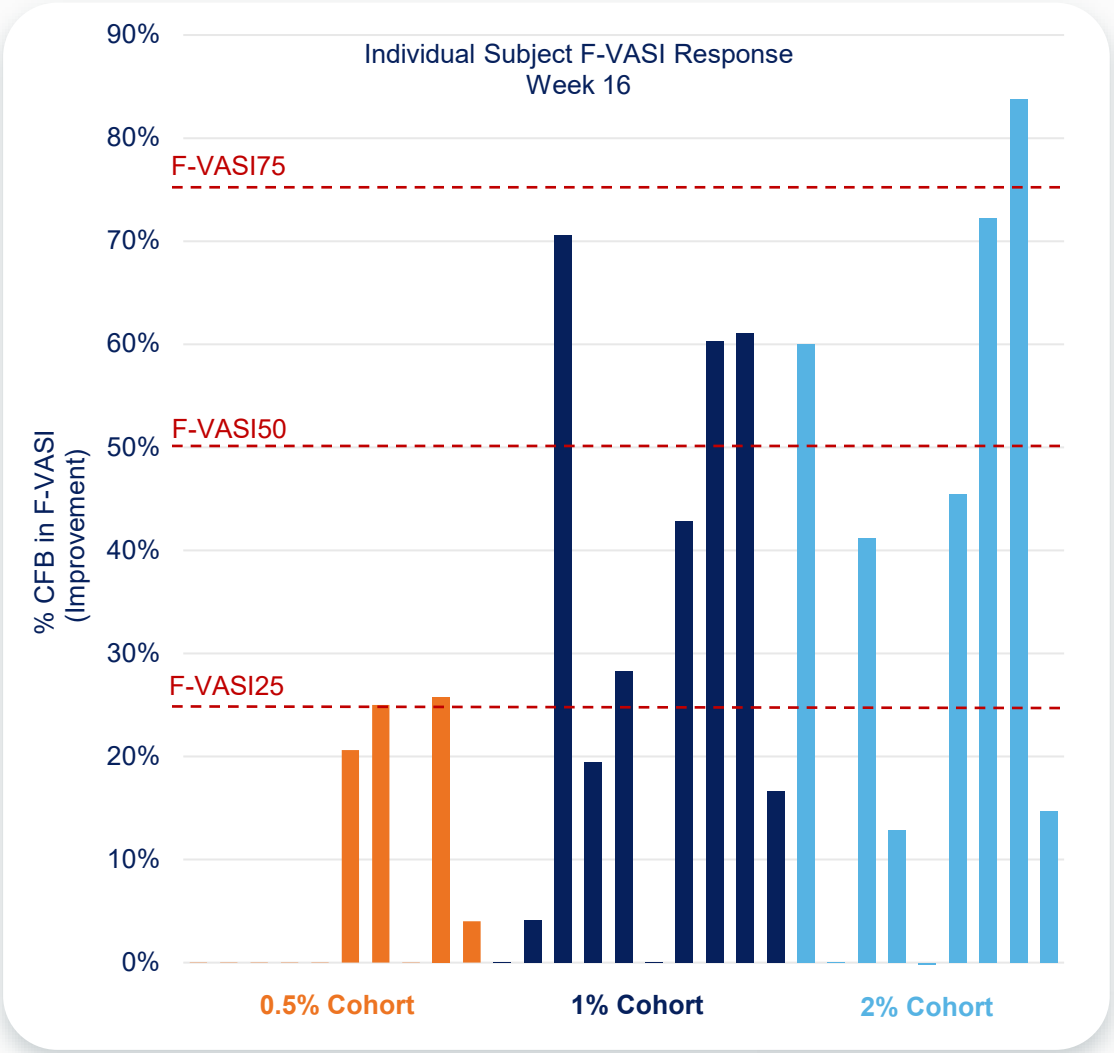
1. **Assess safety, tolerability and pharmacokinetics**
2. **Evaluate VYN201's ability to arrest the progression of depigmentation in active vitiligo patients**
3. **Identify early evidence of repigmentation**
4. **Inform dose level / dose regimen of Phase 2b dose-ranging study**

F-VASI = Facial Vitiligo Area Scoring Index

Promising Onset of Action and F-VASI Response

Repibresib (VYN201) Phase 1b: QD Treatment in 100% active disease study population

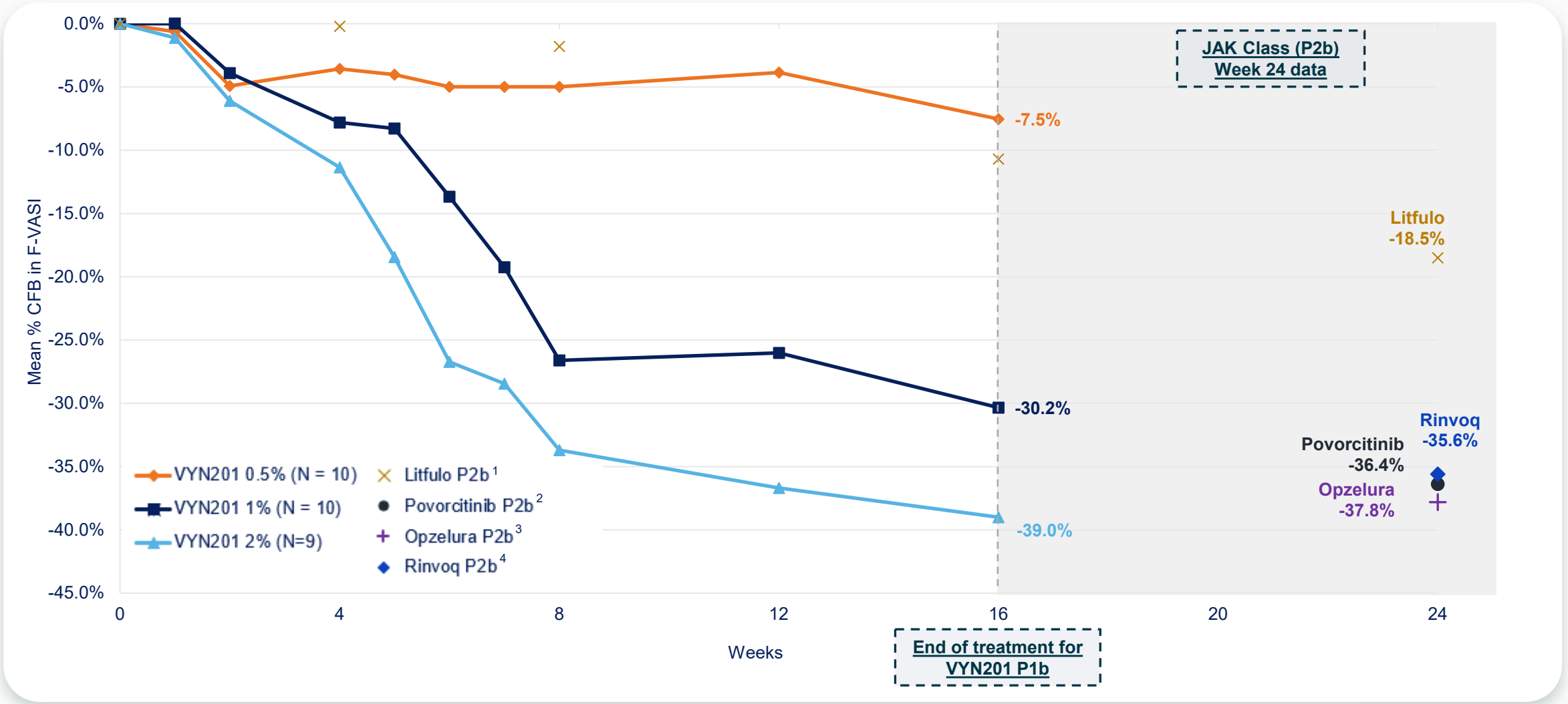




*% CFB T-test based on latest observed case (LOCF)

Demonstrated Competitive Results at 16 Weeks vs. JAK Class at 24 Weeks

Repibresib (VYN201) Phase 1b: QD Treatment in 100% active disease study population



Note: Data is not based on Head-to-Head comparisons; Source: Clinicaltrials.gov; Study Publications: 1. NCT03715829 (LS mean %CFB for 50 mg QD); 2. NCT04818346 (LS mean %CFB for 45 mg QD); 3. NCT03099304 (LS mean %CFB for 1.5% BID); 4. NCT04927975 (LS mean %CFB for 11 mg QD);

Key Takeaways from Repibresib (VYN201) Phase 1b Results

PoC Achieved

- Believed to be first clinical demonstration of BET inhibitor's effect in I&I disease[1]

- Significant clinical response demonstrated with once-daily dosing
- Rapid onset of action with clear evidence of dose response
- Upregulation of WNT pathway observed in skin biopsies and preclinical data

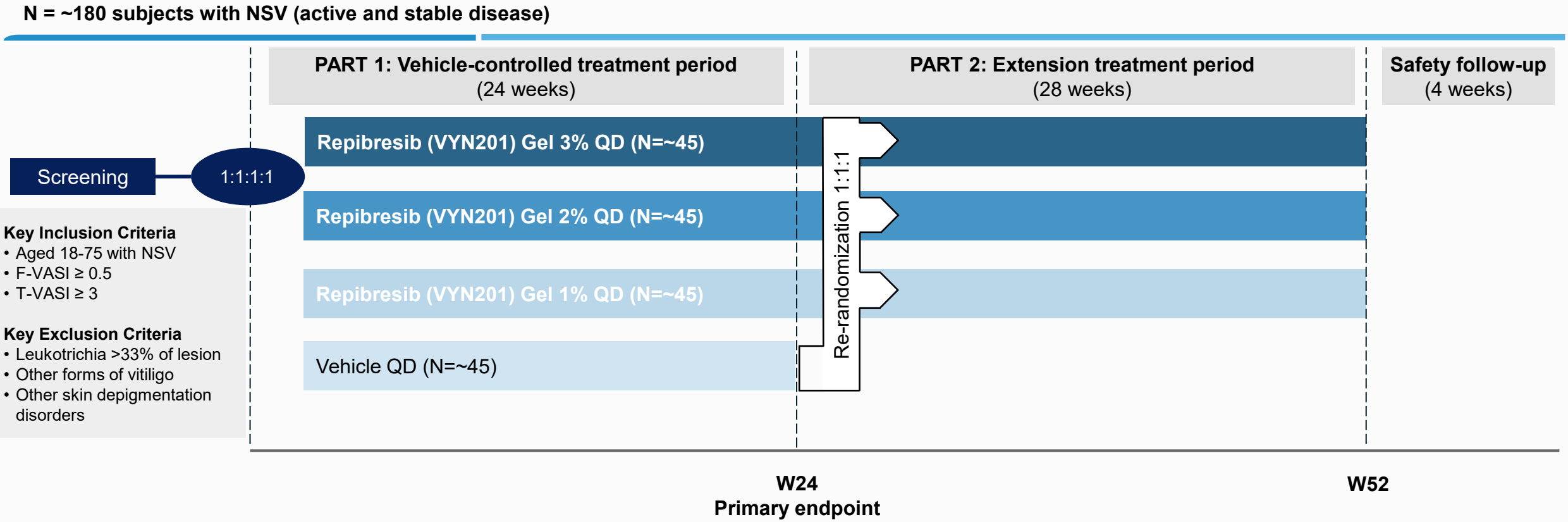
- Demonstrated favorable safety and tolerability profile to date
- Low systemic exposure levels support "soft" drug design

- Data suggest potential to be category leader
- Favorable results compared with the JAK inhibitor competitive landscape

1. Based on readily available public information such as clintrials.gov, academic publications and corporate websites/presentations

Repibresib (VYN201) Phase 2b in Non-Segmental Vitiligo (NSV)

Top-line results from 24-week vehicle-controlled treatment period expected mid-2025



Key Inclusion Criteria
- Aged 18-75 with NSV
- F-VASI ≥ 0.5
- T-VASI ≥ 3

Key Exclusion Criteria
- Leukotrichia >33% of lesion
- Other forms of vitiligo
- Other skin depigmentation disorders

Key safety assessments:

- Treatment emergent adverse events
- Local skin tolerability assessments
- Clinical laboratory assessments, Physical exam/vitals, PK

Key efficacy endpoints:

Primary: Proportion of subjects achieving FVASI50 at Week 24 vs. Vehicle
Secondary: Proportion of subjects achieving TVASI50 at Week 52
Proportion of subjects achieving FVASI25/75 at Week 24 and 52
% CFB in FVASI score at Week 24 and 52

VYN202: BD2 selective BET inhibitor

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VYNE's Drug Design Strategy

Optimize benefit/risk profile of BET inhibitors to target immune-mediated diseases

Repibresib (VYN201)
Pan-BD BET Inhibitor

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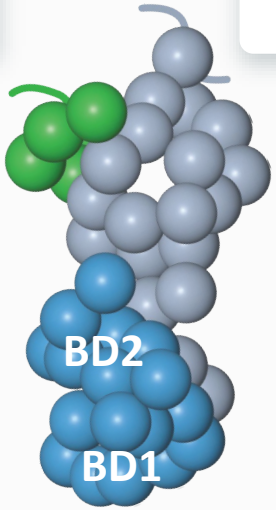


VYN202
BD2-Selective BET Inhibitor

Improve efficacy and tolerability through BD2-selectivity

- Class-leading BD2 vs. BD1 selectivity for systemic administration
- BD2 activity more relevant to inflammatory gene expression
- Minimize BD1 inhibition to protect against steady-state gene disruption

Gilan et al, Science. 2020 April 24; 368(6489): 387–394

 Dawson et al, Science 2020; Belkina, Nikolajczyk & Denis, J. Immunol. 2013

VYN202: A Novel BD2-Selective BET Inhibitor for Immune-Mediated Diseases

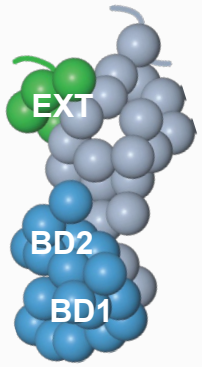
- **VYN202 is an innovative, oral BD2-selective BET inhibitor**
- **VYN202 is believed to be the most potent and BD2-selective BET Inhibitor in clinical development[1] which is designed to improve efficacy and tolerability**
- **Program supported by robust preclinical data across multiple diverse models of immune-mediated disease**
- **Phase 1 SAD and MAD studies in healthy volunteers complete:**
  - VYN202 demonstrated a favorable safety and tolerability profile with no drug-related adverse events historically associated with earlier generation, less selective BET inhibitors
  - Favorable PK profile demonstrated for VYN202, supporting once-daily dosing regimen
  - VYN202 demonstrated robust pharmacodynamic activity including evidence of target engagement and significant inhibition of inflammatory biomarkers relevant to several immune-mediated disorders in ex vivo stimulation assays, consistent with preclinical disease models
- **Promising preliminary data from 7 moderate-to-severe PsO subjects enrolled in Phase 1b PsO trial**
  - All subjects treated with VYN202 had an improvement in signs and symptoms of disease, including scalp psoriasis.
  - Improvements (reduction) in serum cytokine levels involved in the pathogenesis of plaque psoriasis were observed in subjects treated with VYN202 for greater than 1 week, including IL17A, IL17F, IL19 and IL22.
  - Subject treated with VYN202 that co-presented with psoriatic arthritis reported a four-point improvement in joint pain NRS scale by week 2 which corresponded with a reduction in serum c-reactive protein level, a biomarker associated with psoriatic arthritis and other rheumatic diseases.

Compelling data support VYN202's potential as a once-daily oral treatment for serious, immune-mediated diseases with limited treatment options

1. Based on readily available public information such as clintrials.gov, academic publications and corporate websites/presentations.

Drug Design Approach: Maximize On-target Potency and BD2-Selectivity to Optimize the Benefit/Risk Profile of BET Inhibitors

VYN202 is believed to be the most potent and BD2-selective BET Inhibitor in clinical development[1] which is designed to improve efficacy and tolerability



BD2 activity is **associated with inflammatory gene induction** that drives inflammatory responses in autoimmune disease and MPNs

BD1 regulates "housekeeping" gene activity

Compound ID	Potency vs. BD2* (nM)	Selectivity** (BD1/BD2)
VYN202 (VYNE)	**1**	**~10,000**
NUV-868 (Nuvation)[2]	2	1,460x (FRET)
ABBV-744 (AbbVie)[3]	28	753x (FRET)
GSK620 (GSK)[4]	79	220x
INCB057643 (INCY)[5]	6	7x
Pelabresib (NVS/MOR)[2]	17	5x (FRET)
ABBV-075[3]	13	2.6x
MK-8628/OTX-015[6]	26	1.5x
BI-894999[7]	41	0.1x

*Lower number denotes higher potency
**Higher number denotes higher selectivity. Data based on nanoBRET assay unless otherwise indicated.

1. Based on readily available public information such as clintrials.gov, academic publications and corporate websites/presentations. 2. Nuvation corporate presentation (August 2024); 3. Faivre et al 2020; 4. Delmont et al 2020; 5. Pusey, et al. Cancer Res 1 April 2023; 6. Wang et al 2017 7. Kraut et al 2018; Data on file.

VYN202: Phase 1a SAD/MAD Data

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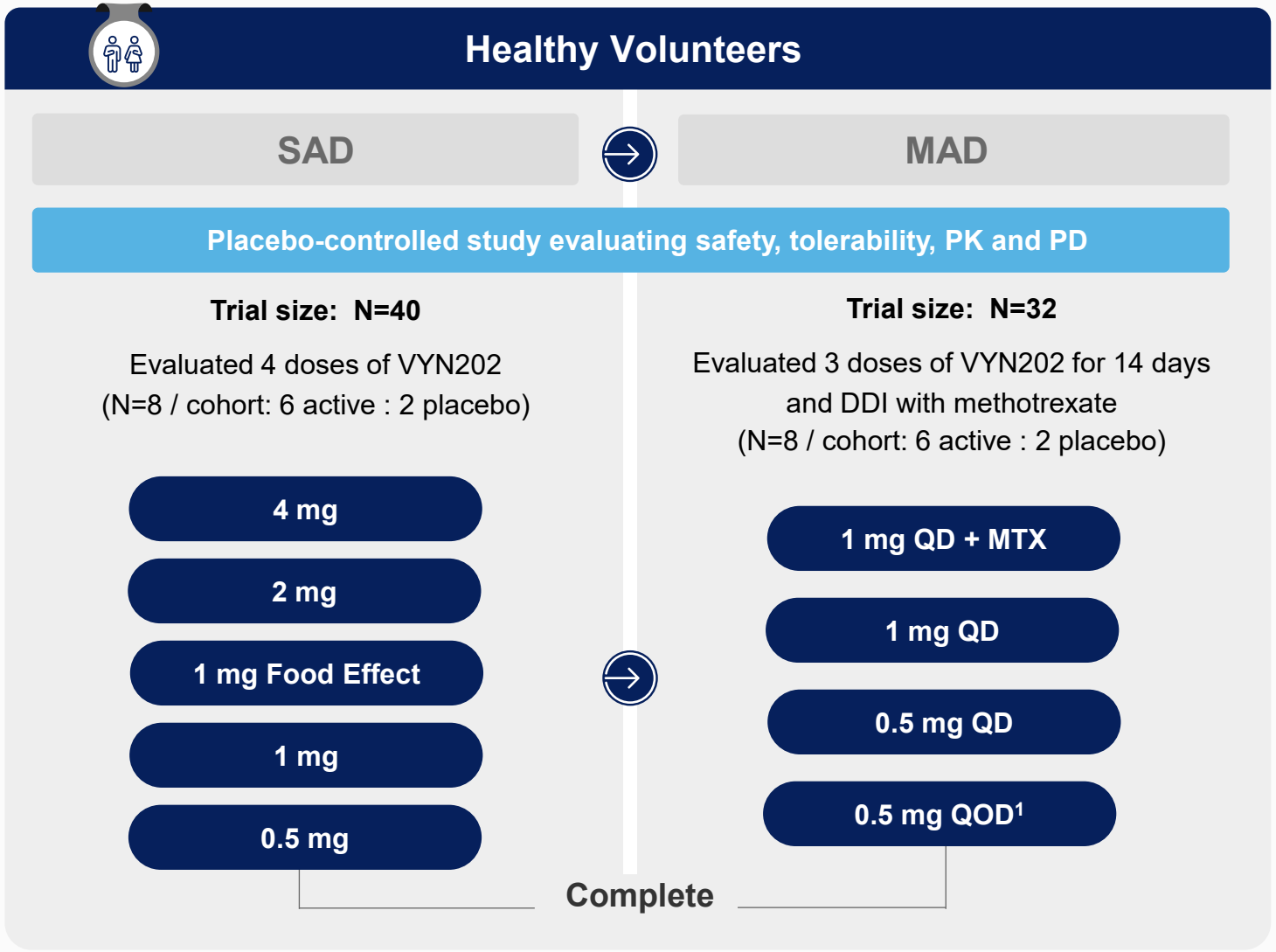
VYN202 Phase 1a SAD/MAD Trial Design and Key Objectives

First-in-human trial in healthy volunteers complete



Key Objectives

Assess:

Safety, Tolerability, Exposure

Exploratory ex vivo pharmacodynamic data:

- Target engagement
- Inflammatory biomarker and cytokine panel

1. Intended to approximate 0.25mg QD dosing; DDI = drug-drug interaction

VYN202 Demonstrated a Favorable Safety and Tolerability Profile in Phase 1

VYN202 was generally well tolerated in Phase 1 MAD with no drug related AEs of special interest historically associated with BET inhibitor class

MAD Results

Treatment Emergent AEs Number of Subjects Reporting (%)	**Placebo** (n=6)	**VYN202**		
		0.5 mg QOD (n=6)	**0.5 mg QD** (n=6)	**1 mg QD** (n=6)
Constipation	2 (33.3)			3 (50.0)
Drowsiness	1 (16.7)		1 (16.7)	
Dysmenorrhea	1 (16.7)		1 (16.7)	
Headache	1 (16.7)			1 (16.7)
Pruritus	1 (16.7)		1 (16.7)	

Safety Findings

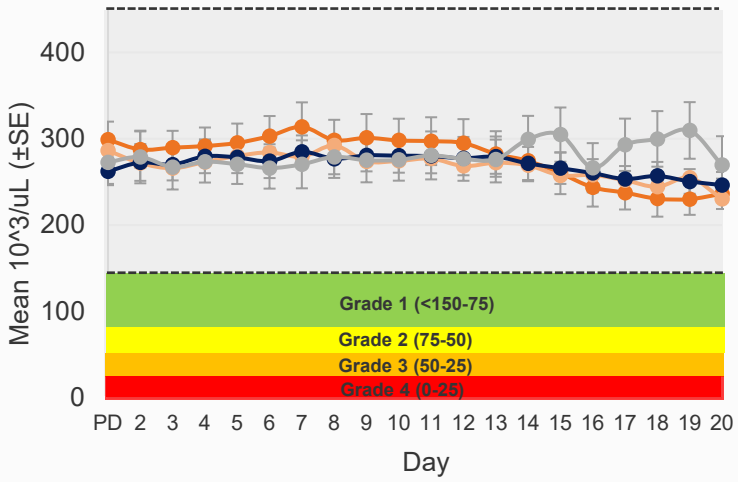
- VYN202 was generally well tolerated
- No serious adverse events or discontinuations due to an AE
- No clinically meaningful treatment emergent AEs
- All treatment emergent AEs considered mild or moderate
- No clinically significant abnormalities in clinical labs or electrocardiogram
- No drug related AEs of special interest historically associated with the BET inhibitor class (thrombocytopenia, neutropenia or gastrointestinal safety findings)

Note: Reported in >1 subject. Excludes those associated with ECG electrode placement and venipuncture reaction

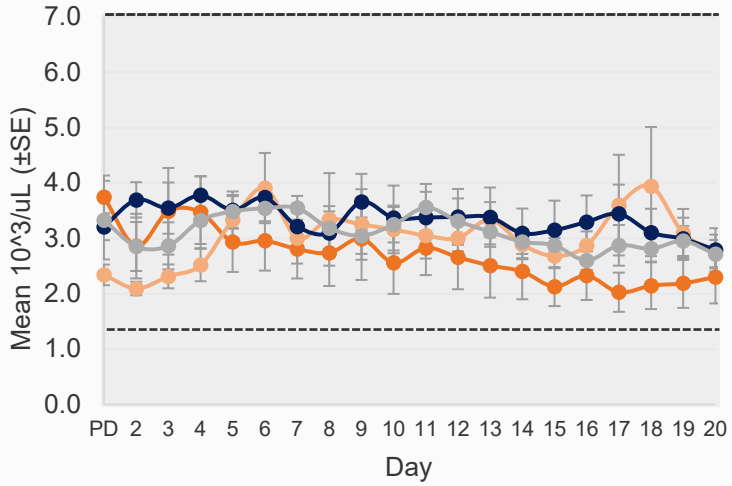
VYN202 Phase 1 MAD Results: Selected Laboratory Data

All laboratory results within normal limits throughout treatment and follow-up period

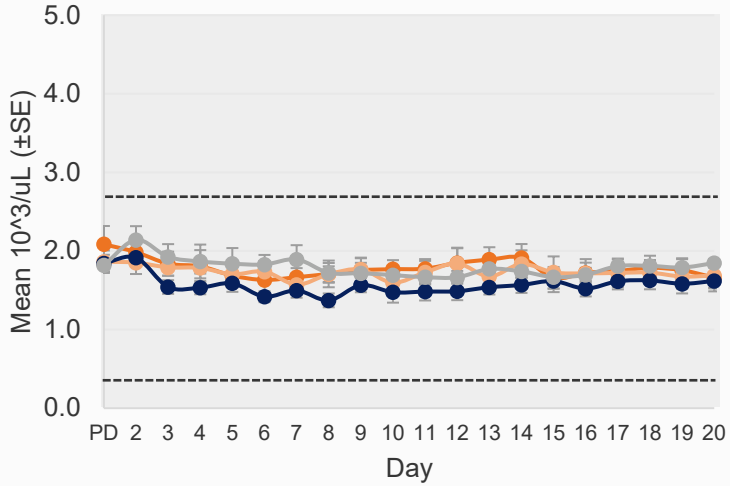
Platelets



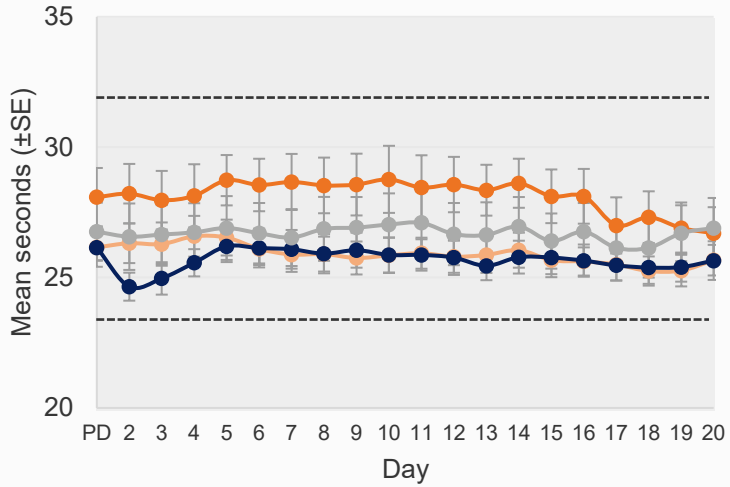
Neutrophils



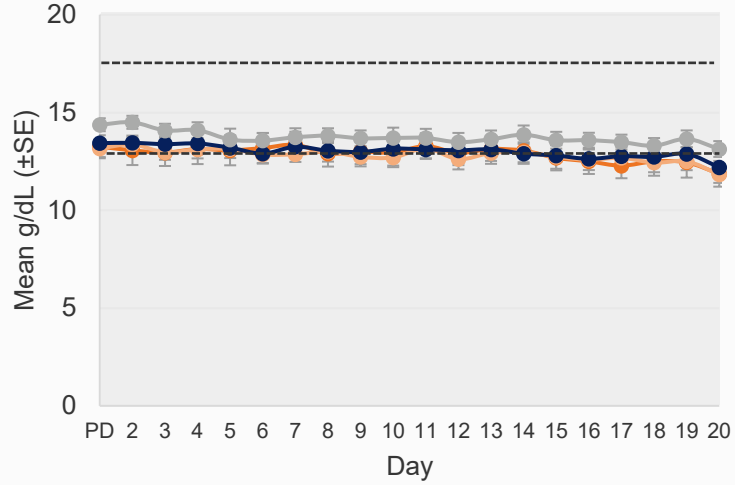
Lymphocytes



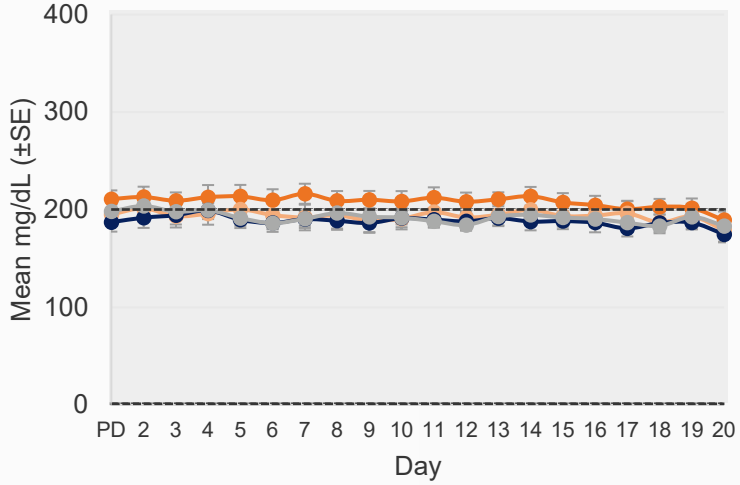
aPTT



Hemoglobin



Cholesterol

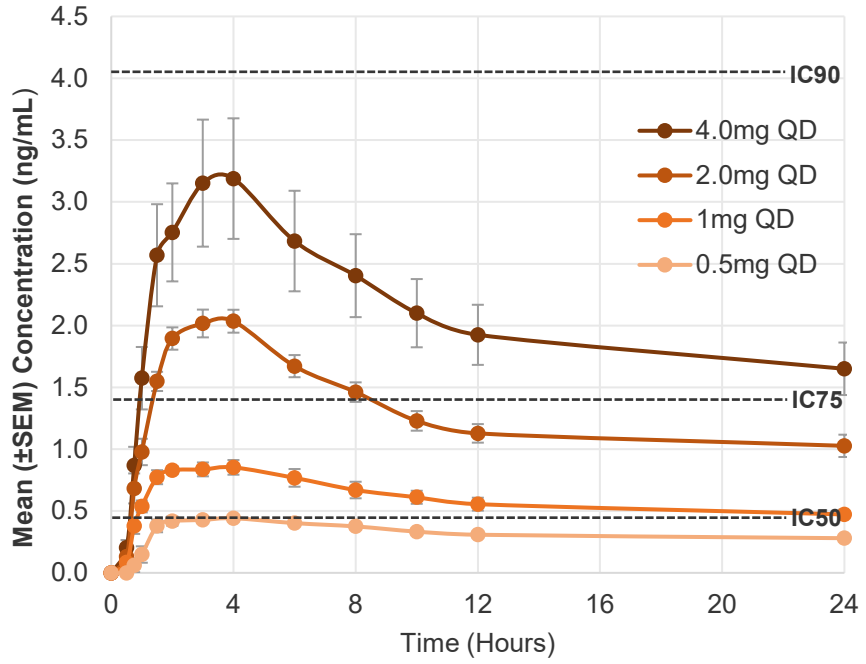


Placebo (n=6) 0.5 mg QOD (n=6) 0.5 mg QD (n=6) 1 mg QD (n=6) ----- Upper/Lower limit of normal

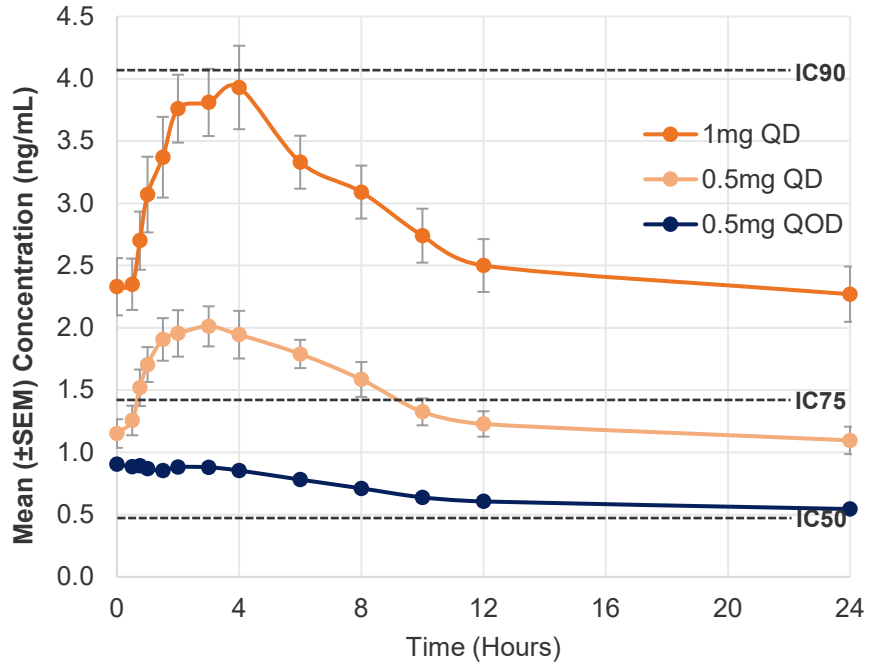
PD=Pre-dose

VYN202 Phase 1 SAD and Day 14 MAD Pharmacokinetics

Single Ascending Dose PK



Multiple Ascending Dose PK, Day 14



- Dose-dependent exposure from dose 0.5 QOD to 4mg, with low variability
- ~4-fold accumulation observed, steady state reached after 7 QD doses
- VYN202 exposure remained above key inhibitory levels vs. BD2 BRD4 for 24 hours post-dose on Day 14
- Median half-life of 36-41 hours supports a once daily dosing posology
- No drug-drug interaction with methotrexate
- Increased exposure with high fat diet

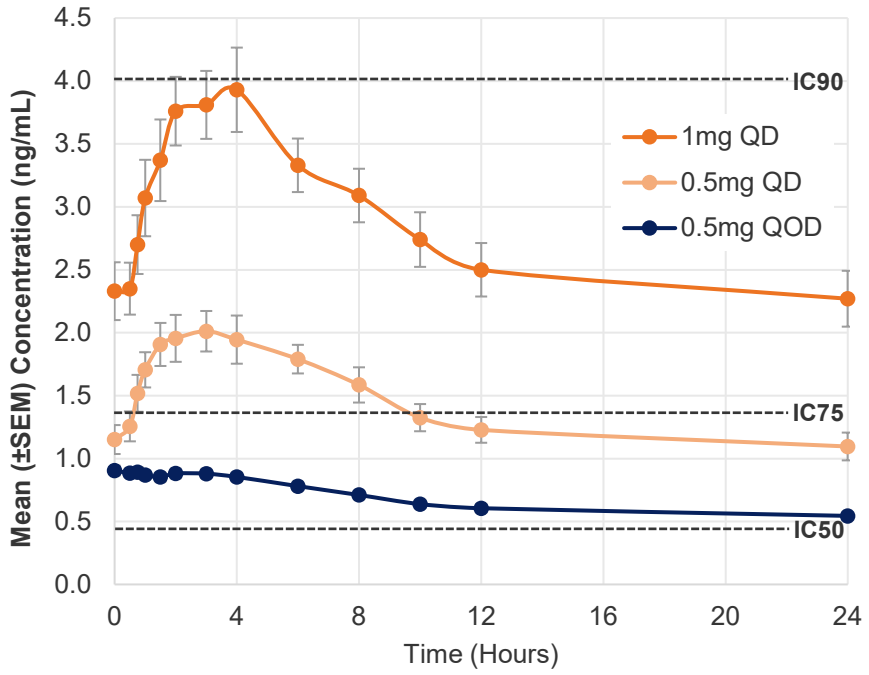
Mean Time Above IC vs. BD2 at Day 14 (hr)		
Dose	IC50	IC75
1 mg QD	>24	>24
0.5 mg QD	>24	~8
0.5 mg QOD	>24	0

IC determined vs. BD2 BRD4 from cell-based nano-BRET assay

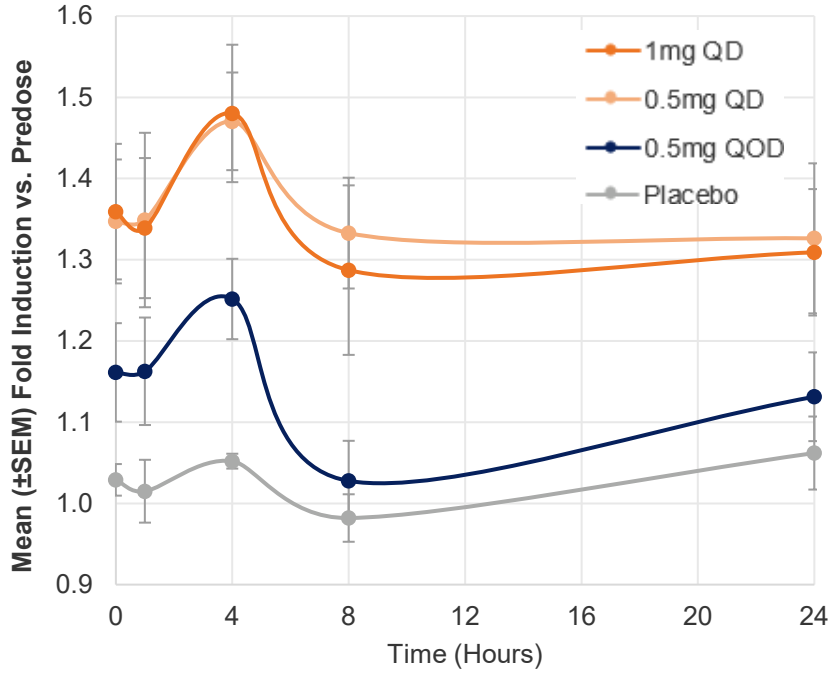
Pharmacokinetics Showed Strong Correlation with Target Engagement

Dose-dependent induction of HEXIM-1 with maximum effect observed at 0.5-1 mg QD

Multiple Ascending Dose PK, Day 14



Multiple Ascending Dose HEXIM-1 Induction, Day 14

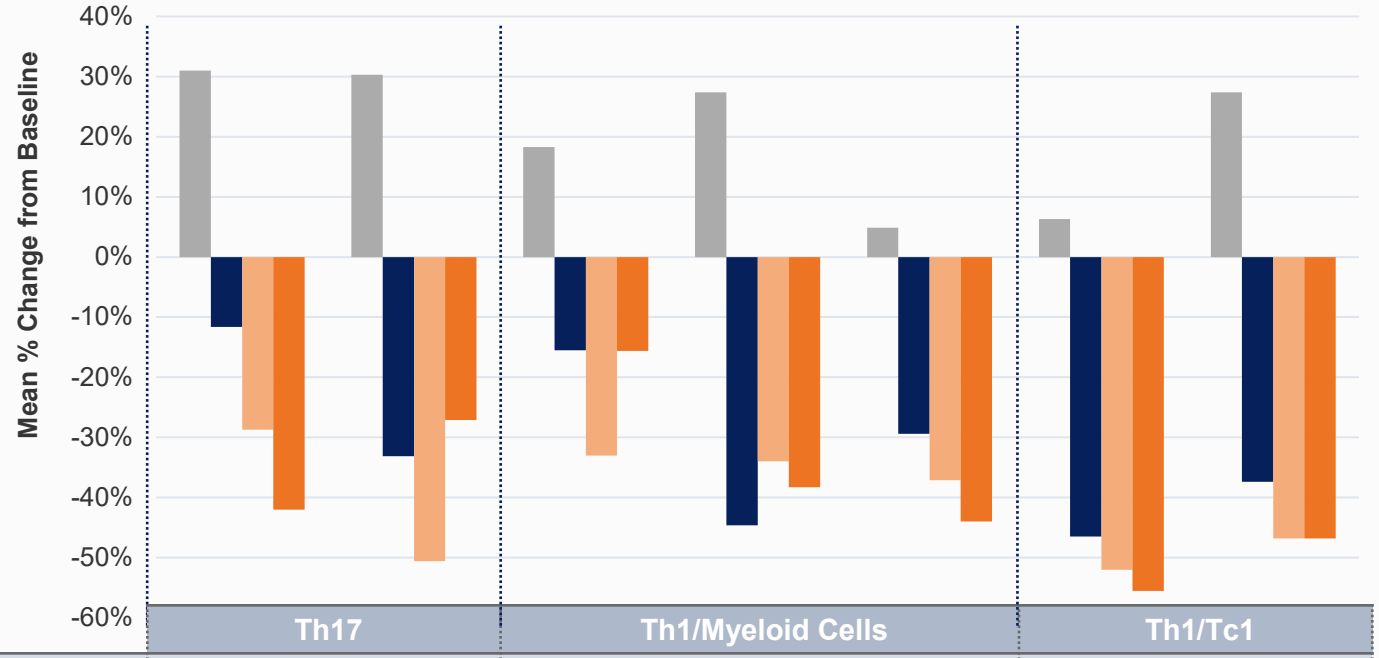


- Inhibition of BET proteins release pTEFb* which activates transcription of pTEFb-dependent genes such as HEXIM-1 leading to higher expression of the HEXIM-1 protein
- Induction of HEXIM-1 closely follows corresponding pharmacokinetics of VYN202 (Tmax: ~4hrs)

pTEFb: positive transcription elongation factor-b

Demonstrated Impact on Pro-Inflammatory and Disease Related Cytokines

Ex Vivo Inhibition of Disease Related Cytokines[1], Day 14



	Th17		Th1/Myeloid Cells			Th1/Tc1	
cytokines	IL-17 (%)	IL-23 (%)	IL-1β (%)	TNF (%)	IL-6 (%)	IFNγ (%)	CXCL10 (%)
Placebo (n=6)	31	30	18	27	5	6	27
0.5mg QOD (n=6)	-12	-33	-16	-45	-29	-47	-37
0.5 mg QD (n=6)	-29	-51	-33	-34	-37	-52	-47
1 mg QD (n=6)	-42	-27	-16	-38	-44	-56	-47
Max Δ vs placebo	-73	-81	-51	-72	-49	-62	-74

Significant inhibition of key cytokines relevant to several immune-mediated diseases

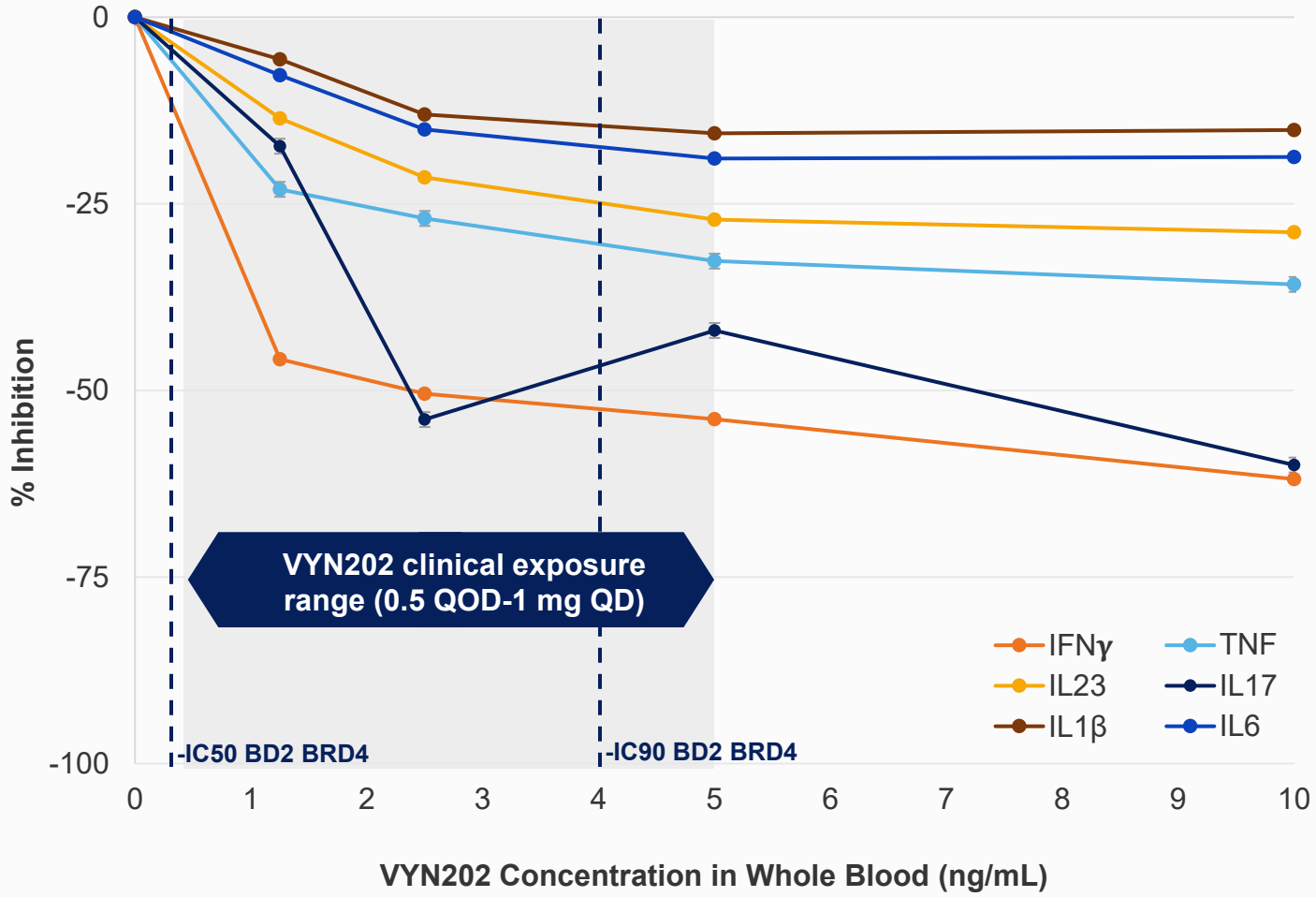
Comparable inhibitory effects to that demonstrated in preclinical efficacy models

Emerging relationship between VYN202 exposure, HEXIM-1 induction and cytokine inhibition

1Using TLR4/TLR7 stimulation and analysis from whole blood samples

Majority of Cytokine Suppression Occurred in Concentrations at 1 mg or Below

in preclinical in vitro tests at fixed concentrations of VYN202 ranging from 0 to 10 ng/mL



VYN202 exhibited steep exposure/response curves, consistent with preclinical disease models

Majority of inhibitory effect occurred at exposures equivalent to 0.25 mg QD[1] to 1 mg QD dosing of VYN202 (0 to 5 ng/mL)

Minimal additional inhibitory benefit with increased exposure beyond 5ng/mL

1. 0.5mg QOD intended to approximate 0.25mg QD dose
2. Mean clinical concentration range of VYN202 is approximately 0.5 ng/mL (0.5mg QOD trough concentration at steady state) to approximately 5 ng/mL (1 mg Cmax at steady state).

VYNE™ THERAPEUTICS

VYN202 Phase 1a MAD Data Summary

Safety

- Demonstrated favorable safety and tolerability profile
- No drug-related adverse events historically associated with earlier generation, less selective BET inhibitors, including thrombocytopenia, neutropenia or gastrointestinal toxicity findings
- No serious adverse events (AEs), discontinuations due to an AE or clinically meaningful treatment emergent adverse events (TEAEs)
- All TEAEs were considered mild or moderate in severity
- No drug-related adverse events associated with laboratory results

Pharmacokinetics

- Favorable PK profile
- Data supports once-daily dosing regimen
- VYN202 demonstrated dose dependent exposure that reached steady-state after 7 once-daily doses
- VYN202 blood levels were within key inhibitory thresholds of IC50 to IC90 against BD2 BRD4 for at least 24 hours at all doses
- No drug-drug interaction observed when VYN202 was co-administered with methotrexate, a treatment commonly used in the management of chronic immuno-inflammatory conditions

Pharmacodynamics

- Robust pharmacodynamic activity on target engagement and inflammatory biomarkers in ex vivo assays
- VYN202 induced a dose-dependent increase in the target engagement biomarker HEXIM-1 with a maximal effect observed at 0.5mg to 1 mg QD
- VYN202 inhibited the production of multiple inflammatory biomarkers related to Th17, Th1/myeloid and Th1/Tc dysregulated activity, consistent with preclinical models of VYN202
- VYN202 exhibited steep exposure/response curves, consistent with preclinical disease models, with majority of inhibitory effect occurring at exposures equivalent to 0.25 mg QD to 1 mg QD dosing of VYN202 (0 to 5 ng/mL)

VYN202:
Phase 1b Moderate-to-Severe PsO

VYNE™ THERAPEUTICS

VYN202 Phase 1b Study Design in Moderate-to-Severe Plaque Psoriasis

No longer enrolling or dosing patients in study - 7 subjects enrolled

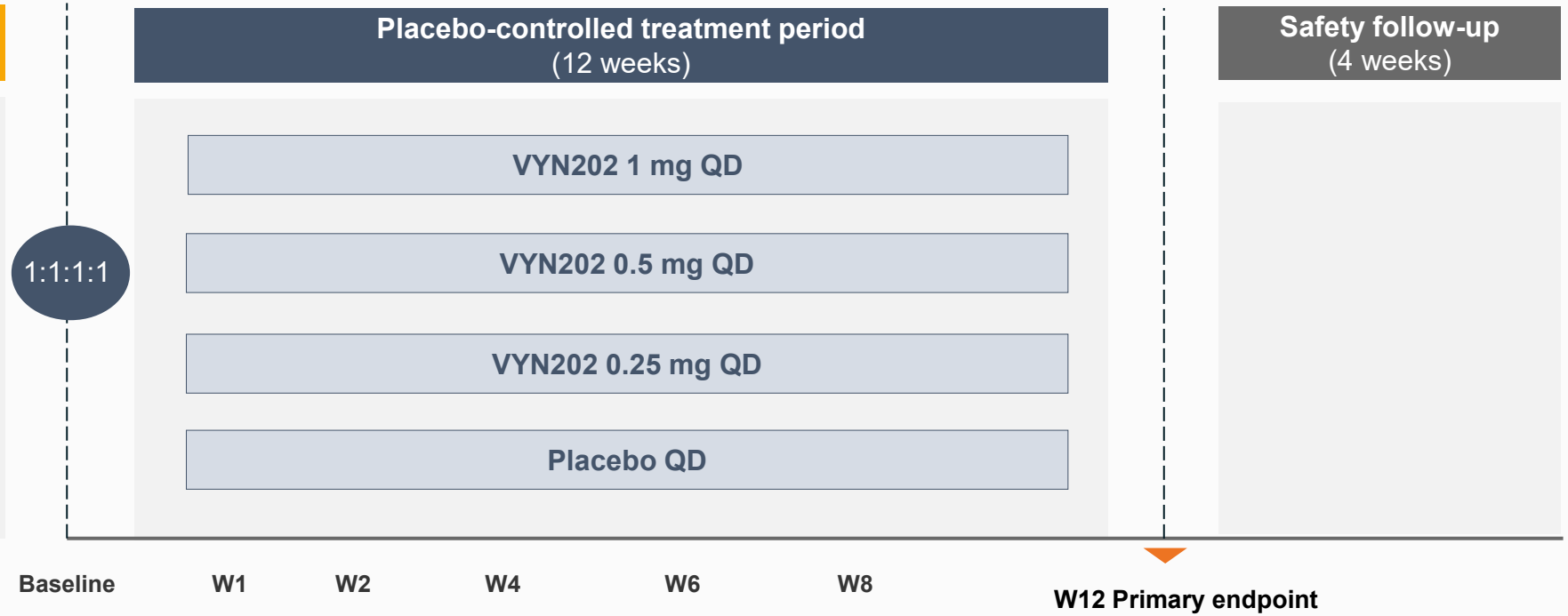
Screening period
(30 days)

Key Inclusion Criteria

- 18-75 y
- BMI 18-40
- PASI ≥ 12
- sPGA≥ 3
- BSA ≥ 10%
- Biologic experienced capped at 30%

Key Exclusion Criteria

- Other forms of psoriasis
- Recent infections
- Concomitant immunomodulators



Key safety / PK assessments:	Treatment emergent adverse events Physical exam/vitals Clinical laboratory assessments Cmin, Cave, AUC
Key efficacy endpoints: (exploratory)	***Primary:*** Change from baseline in PASI; PASI 75 ***Secondary:*** PASI 90, PASI 100, sPGA 0/1, Scalp measures, DLQI; Biomarker Analysis

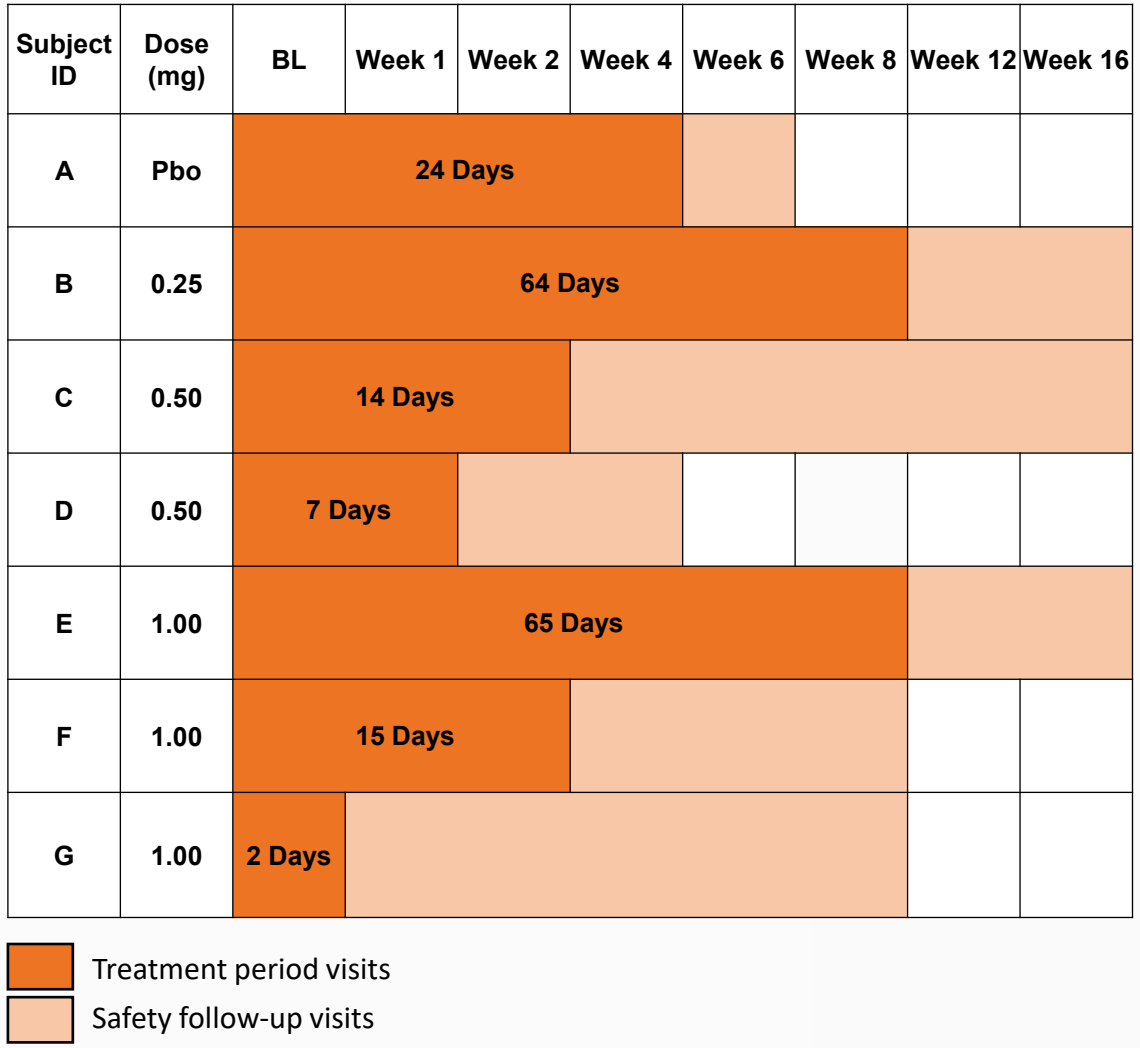
- In April, the FDA placed a clinical hold on the Company's Phase 1b trial following an observation of testicular toxicity in dogs from a non-clinical toxicology study of VYN202.
- In June, the FDA lifted the clinical hold for female patients on the 0.25 mg and 0.5 mg doses. The 1 mg dose was not included at this time in the revised psoriasis protocol submitted to the FDA due to its lower toxicological safety margin as compared to the 0.25 mg and 0.5 mg doses.

VYN202 Phase 1b Study: 7 Patients Enrolled

Demographic and Patient Characteristics

Parameter	Value
Mean Age, yr (min-max)	47.1 (30-59)
Sex, M/F	5/2
Race	White (7)
Ethnicity, HL / nHL	3/4
Mean PASI at Baseline (min-max)	18.3 (12.1-36.7)
Mean PSSI at Baseline (min-max)	20.0 (3-54)
Mean sPGA at Baseline (min-max)	3.1 (3-4)
Mean %BSA at Baseline (min-max)	20.8 (10-37)

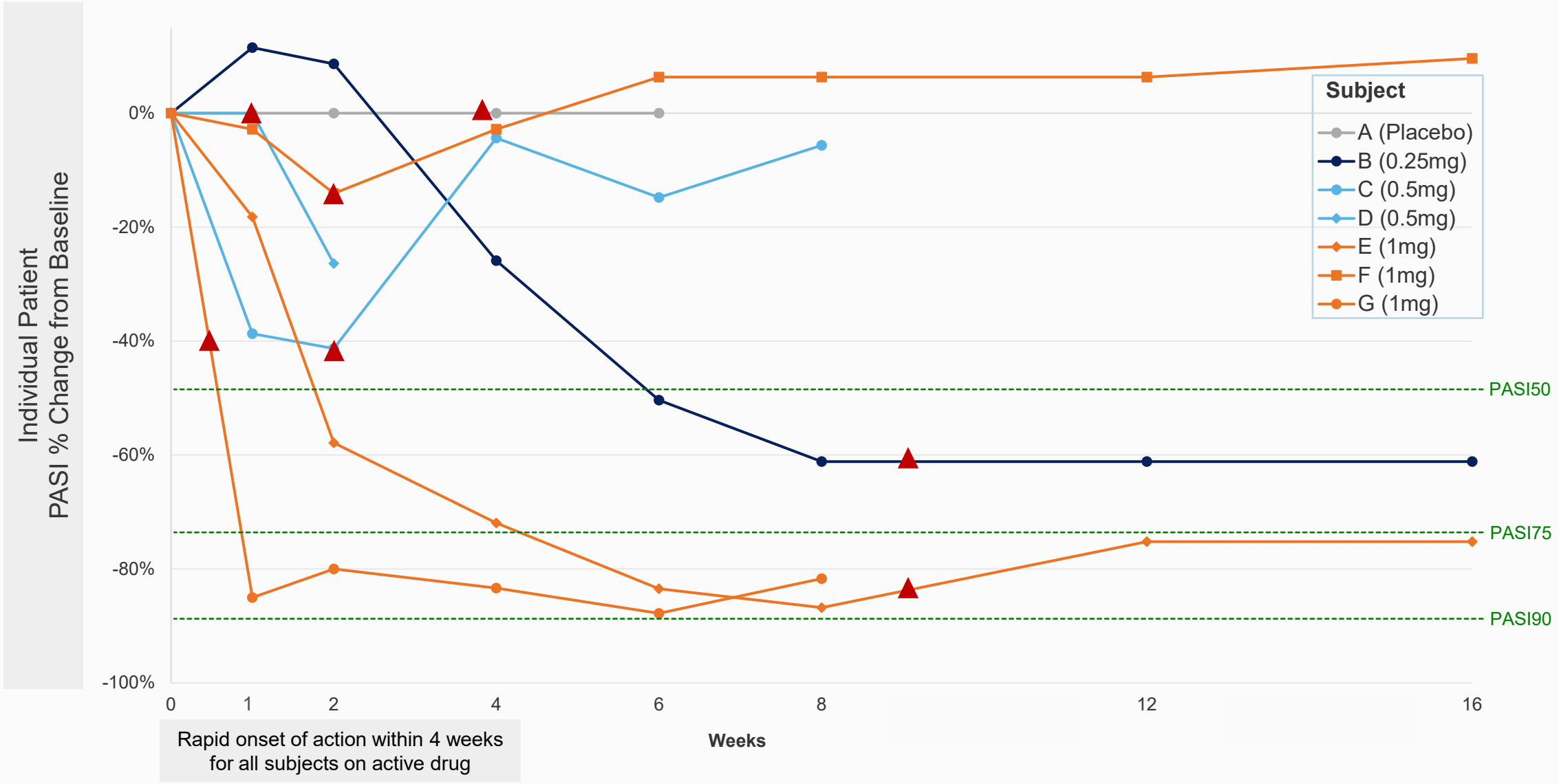
Duration of treatment



Preliminary Data available as of 6/20

HL - Hispanic or latino; nHL - not Hispanic or Latino

Individual PASI Score Changes



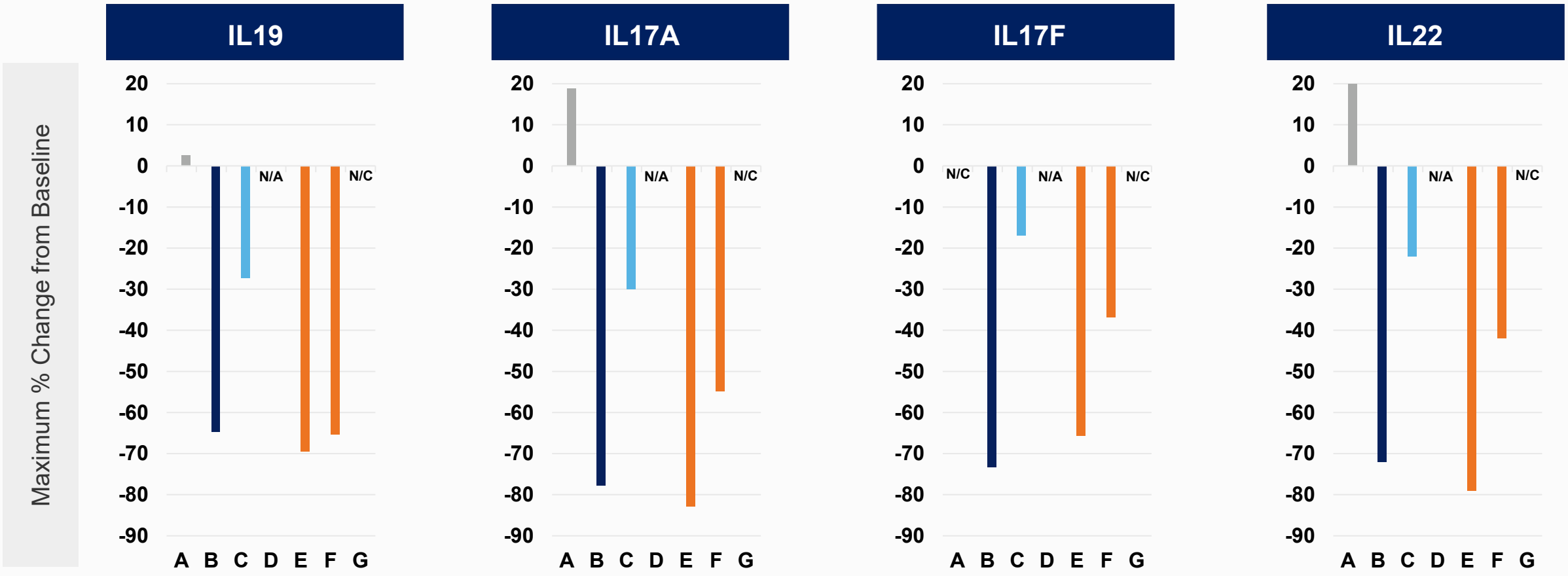
Rapid onset of action within 4 weeks for all subjects on active drug

▲ Last dose

Letters A-G represent Patient ID

Preliminary Data available as of 6/20

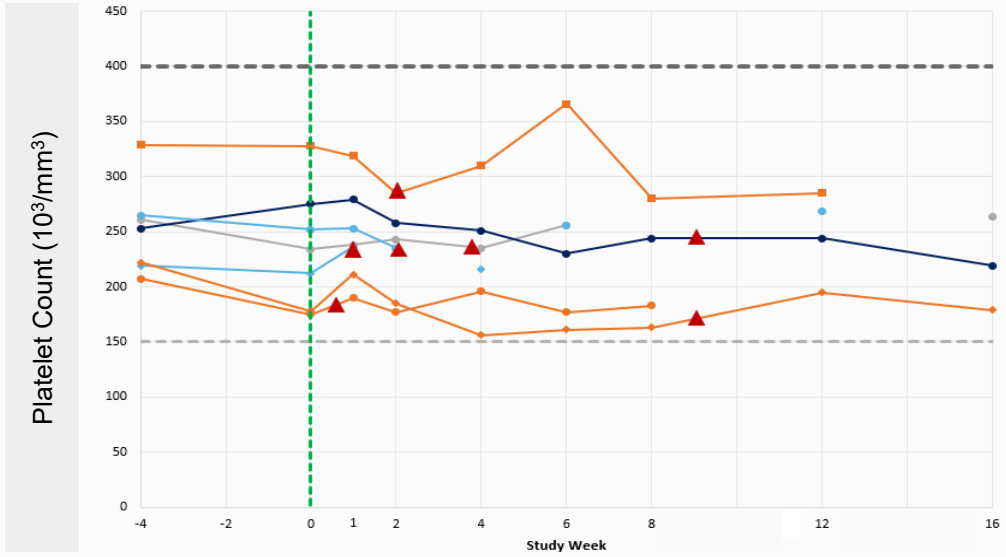
Serum Inflammatory Biomarkers



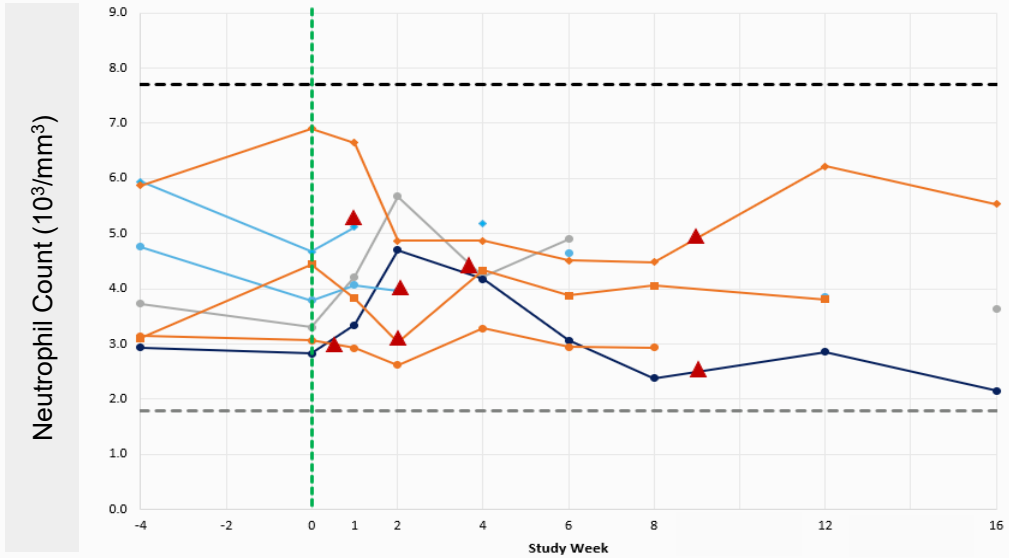
- Reduction in serum cytokine levels observed in subjects treated with VYN202 for greater than 1 week ranging from -17% to -83%. No change in these serum cytokines for the subject receiving placebo (Subj. A).
- Subject C treated with VYN202 0.5 mg with a medical history of psoriatic arthritis reported a four-point improvement in joint pain NRS scale by week 2 corresponding with a -48% reduction in serum c-reactive protein level. Subject A treated with placebo with a medical history of psoriatic arthritis had no improvement in joint pain NRS and no change in serum c-reactive protein levels.

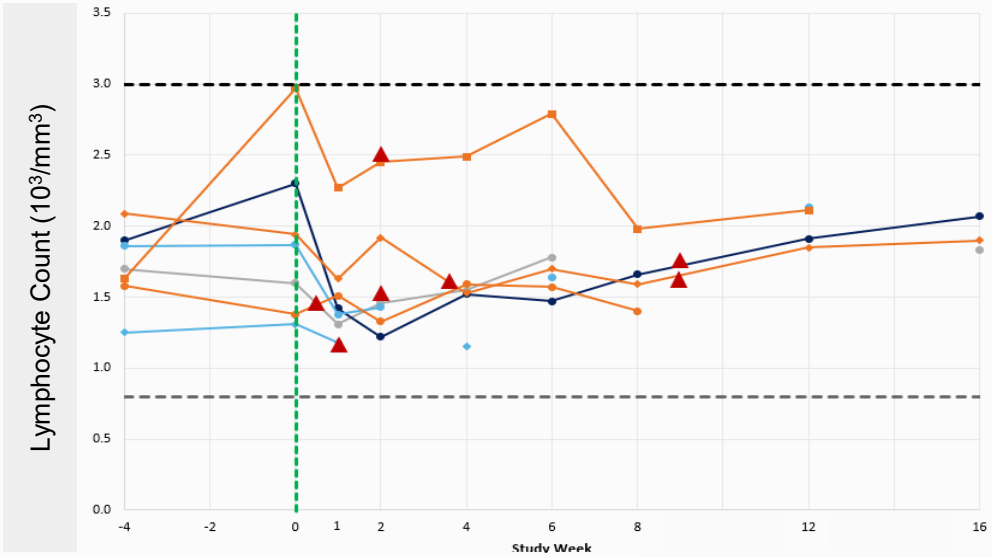
Preliminary Data available as of 6/30; N/A – Data not available; N/C – No change; Percent change from baseline: 1-[Lowest value during treatment / Baseline value] * 100%

Selected Laboratory Data



- All data within Upper and Lower Limits of Normal (ULN/LLN)
- No grades of thrombocytopenia and trends in platelet counts reach a nadir between 4 and 6 weeks and increase during treatment
- No grades of Neutropenia
- No grades of lymphopenia





Baseline visit ▲ Last dose ----- Upper/Lower limit of normal

A (Placebo) B (0.25mg) C (0.5mg) D (0.5mg) E (1mg) F (1mg) G (1mg)

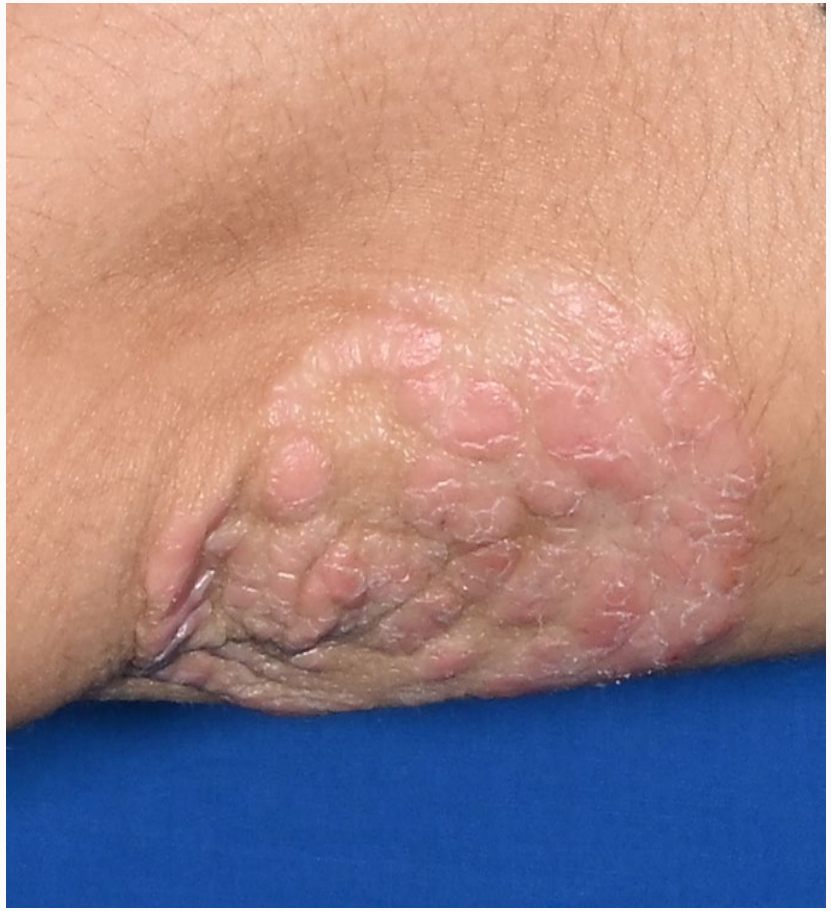
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

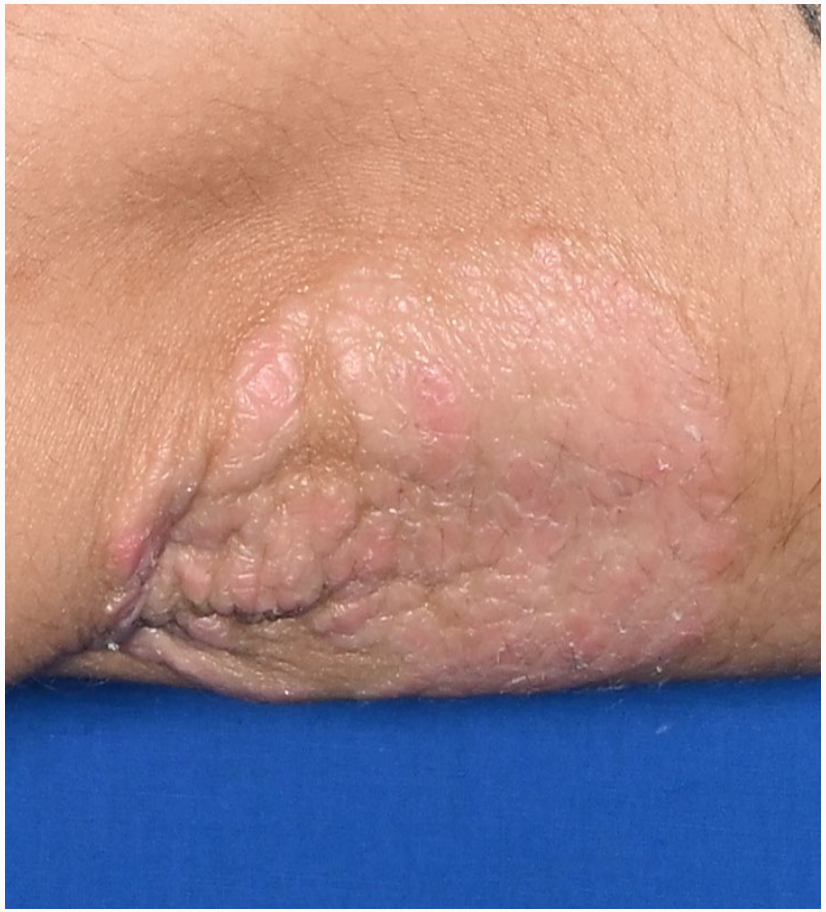
Last Dose Administered Day 64

Right Elbow

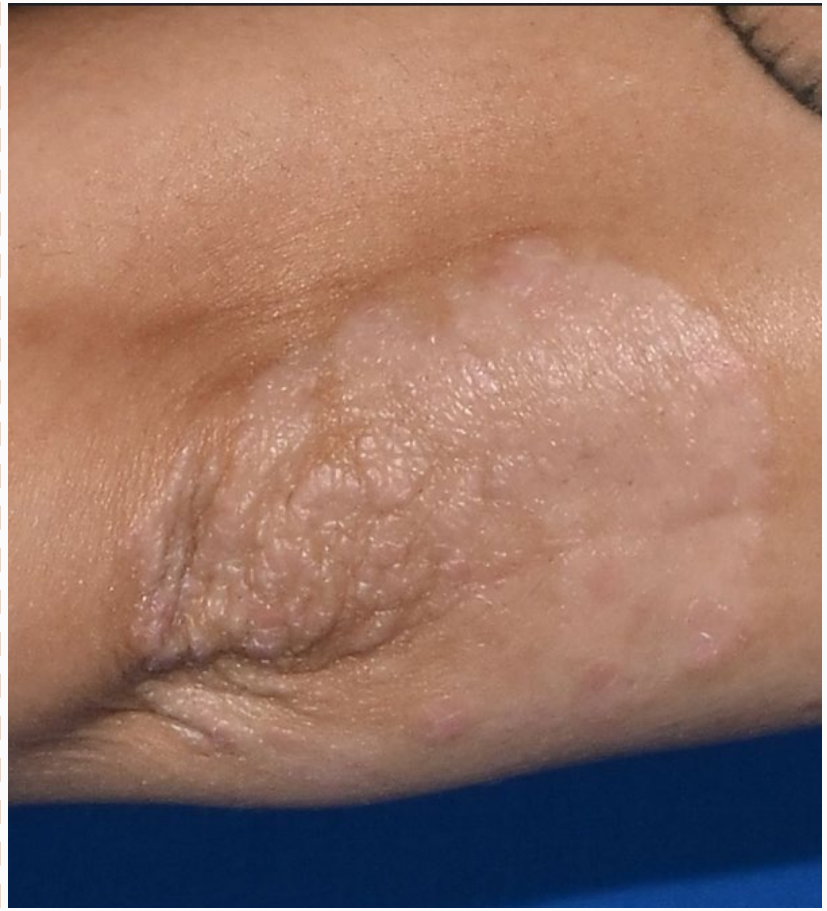
Day 1
(PASI 13.9)



Week 6
(PASI 6.9)



Week 12
(PASI 5.4)



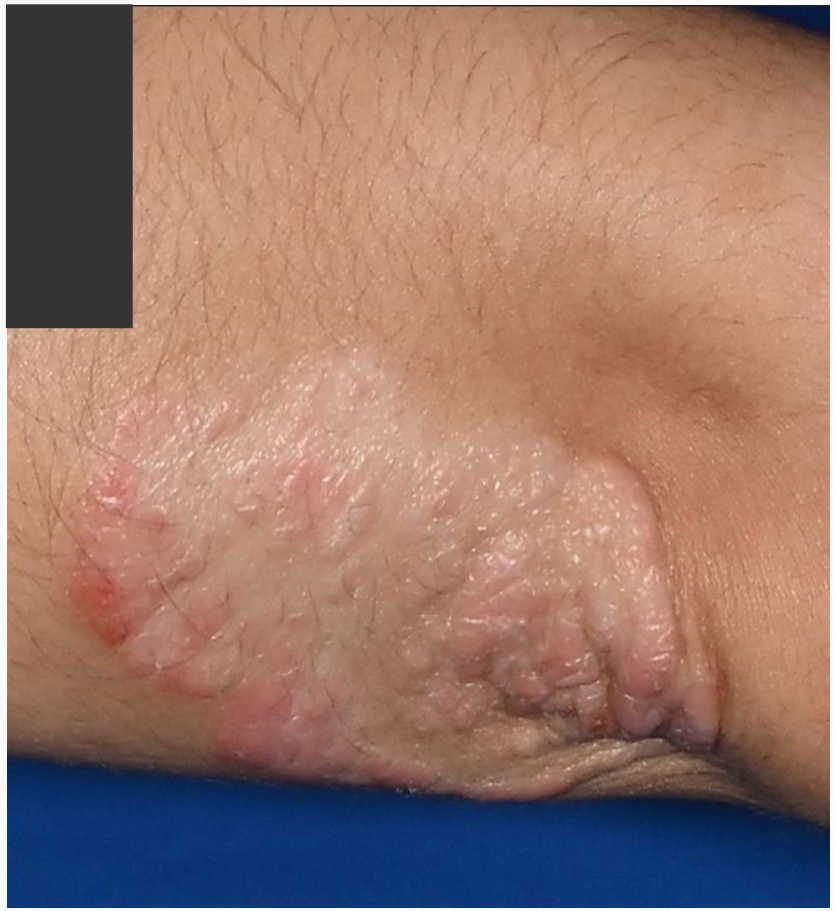
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

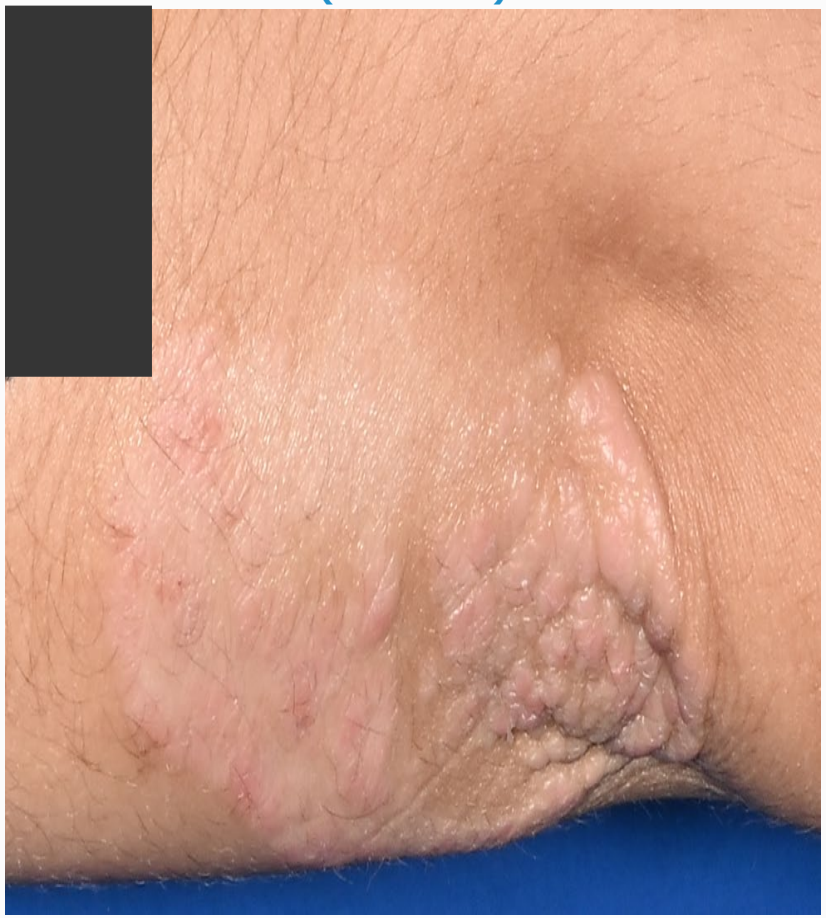
Last Dose Administered Day 64

Left Elbow

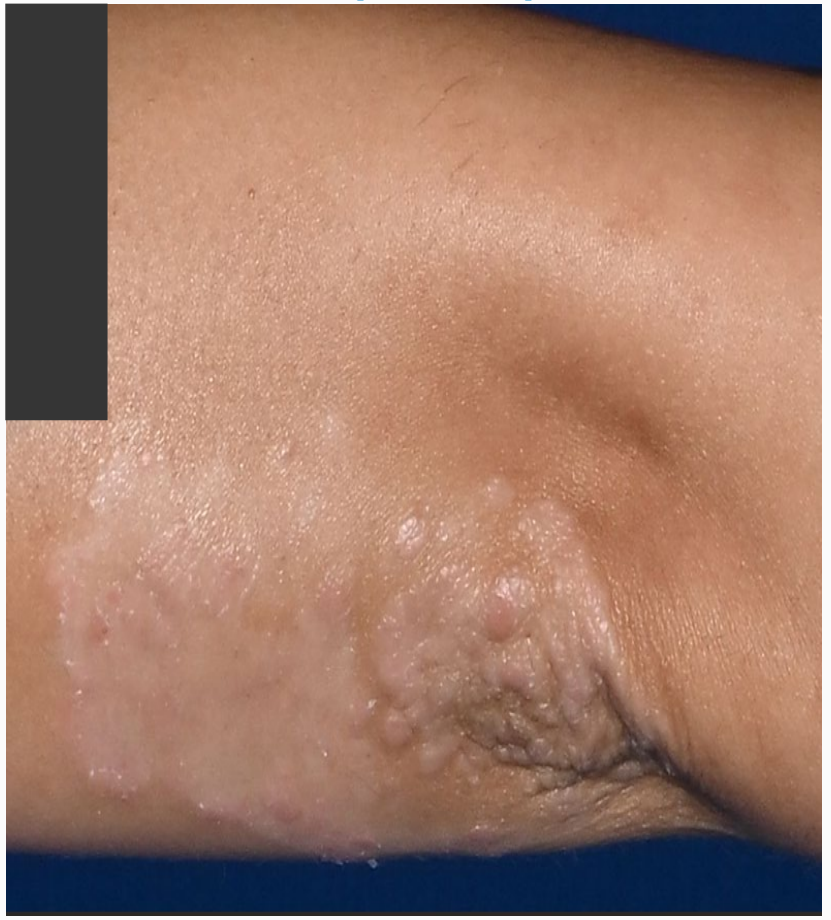
Day 1
(PASI 13.9)



Week 6
(PASI 6.9)



Week 12
(PASI 5.4)



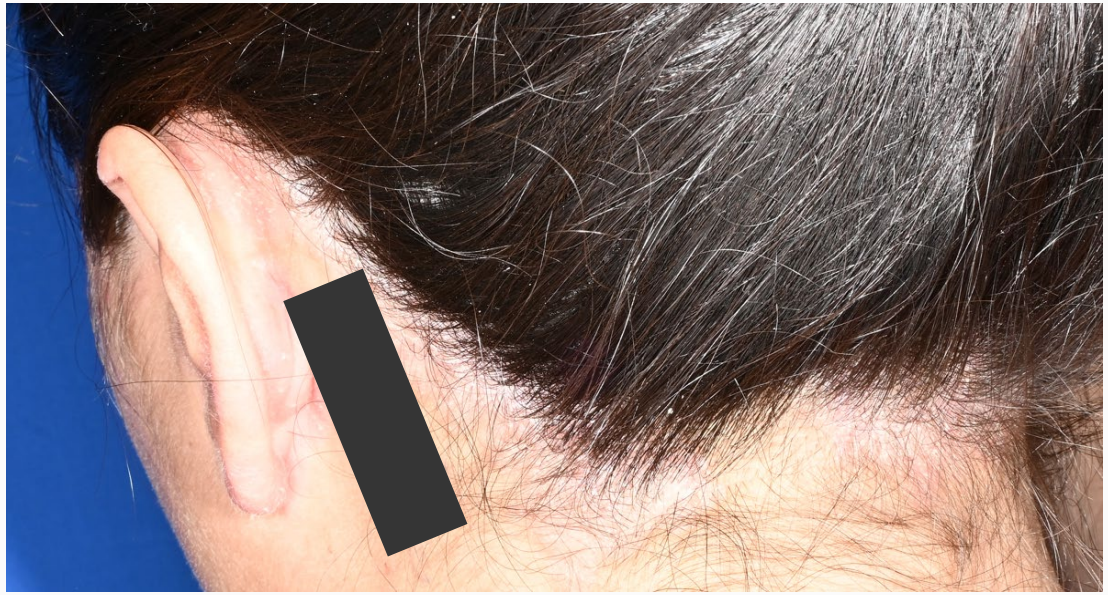
Visual Improvements in Psoriasis in 6 weeks

Subject B (0.25mg)

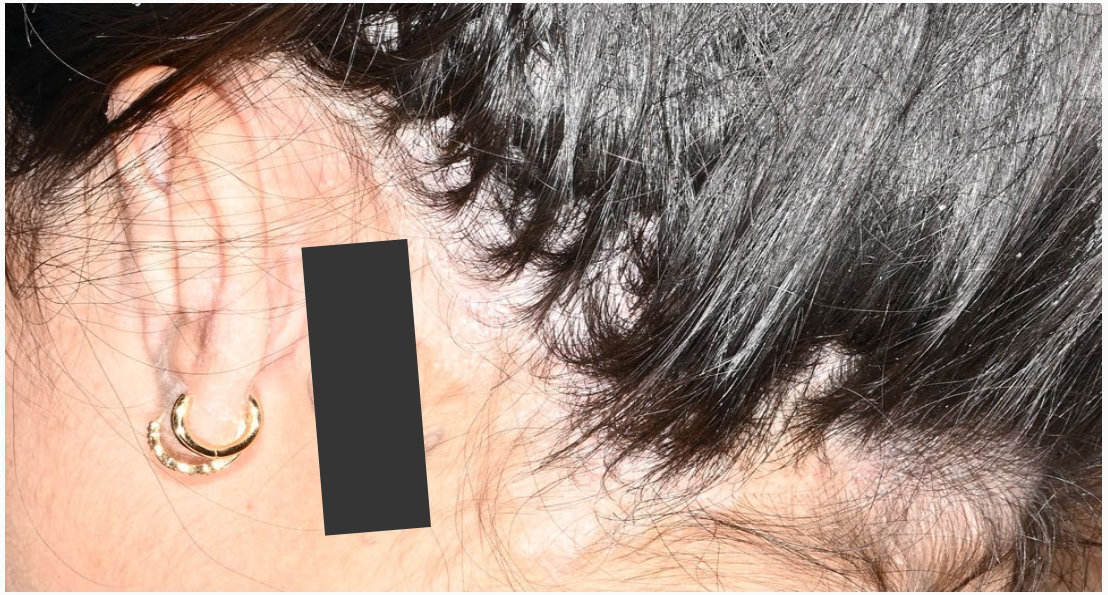
Back Scalp

Day 1
(PSSI 14)

Week 6
(PSSI 4)



Week 12
(PSSI 1)



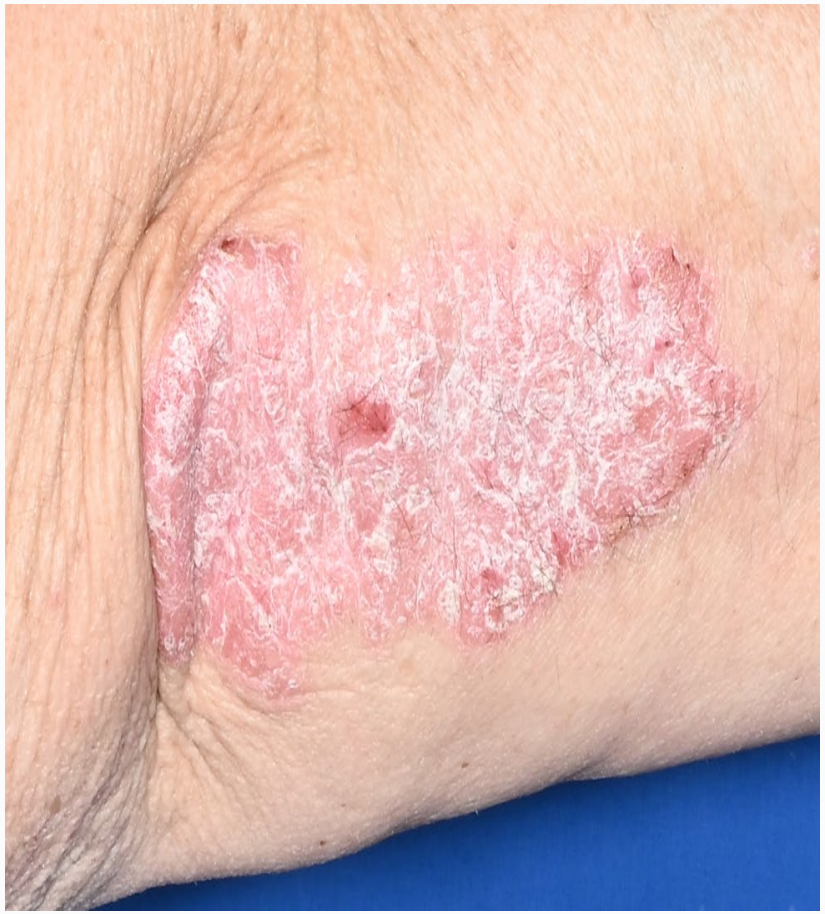
Visual Improvements in Psoriasis in 6 weeks

Subject E (1mg)

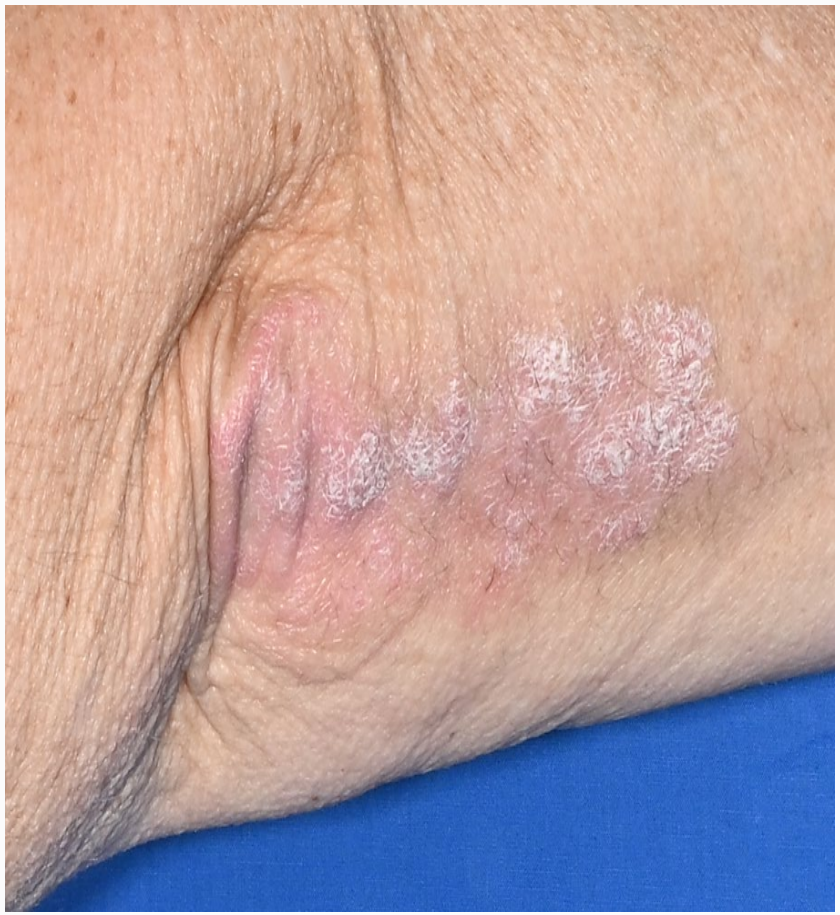
Last Dose Administered Day 65

Right Elbow

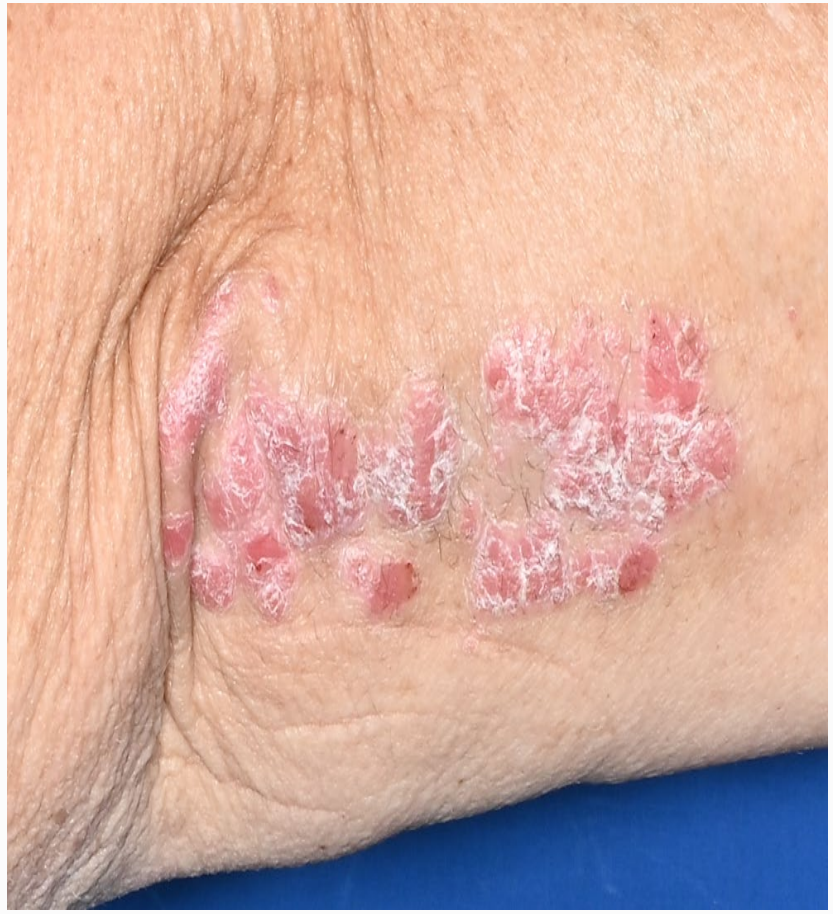
Day 1
(PASI 12.1)



Week 6
(PASI 2.0)



Week 12
(PASI 3.0)



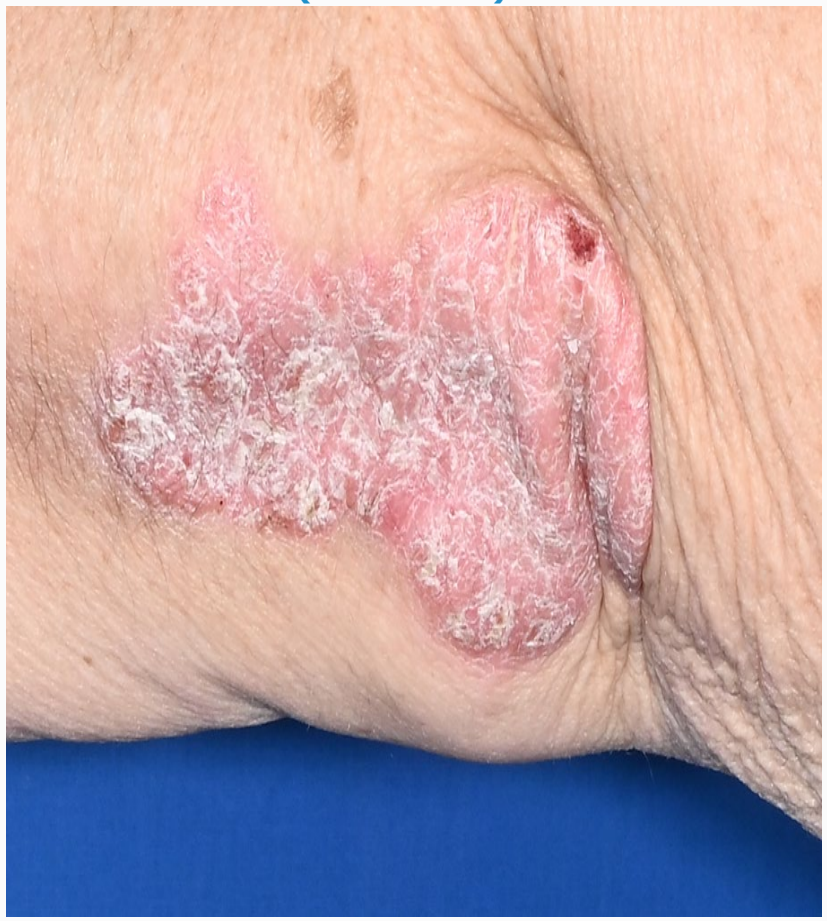
Visual Improvements in Psoriasis in 6 weeks

Subject E (1mg)

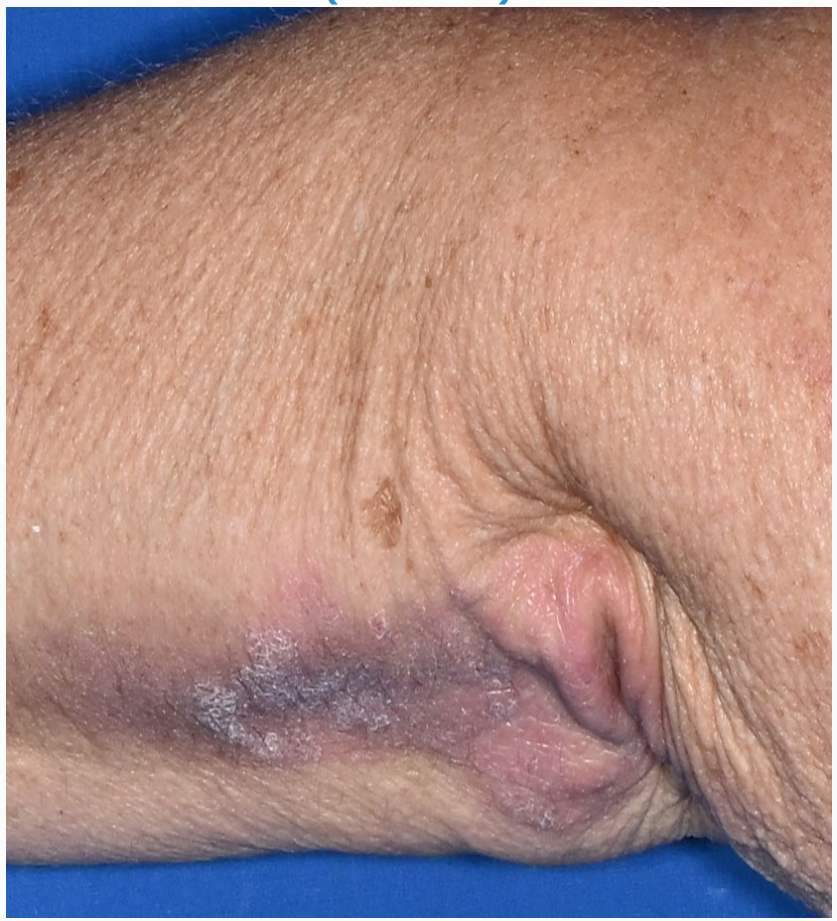
Last Dose Administered Day 65

Left Elbow

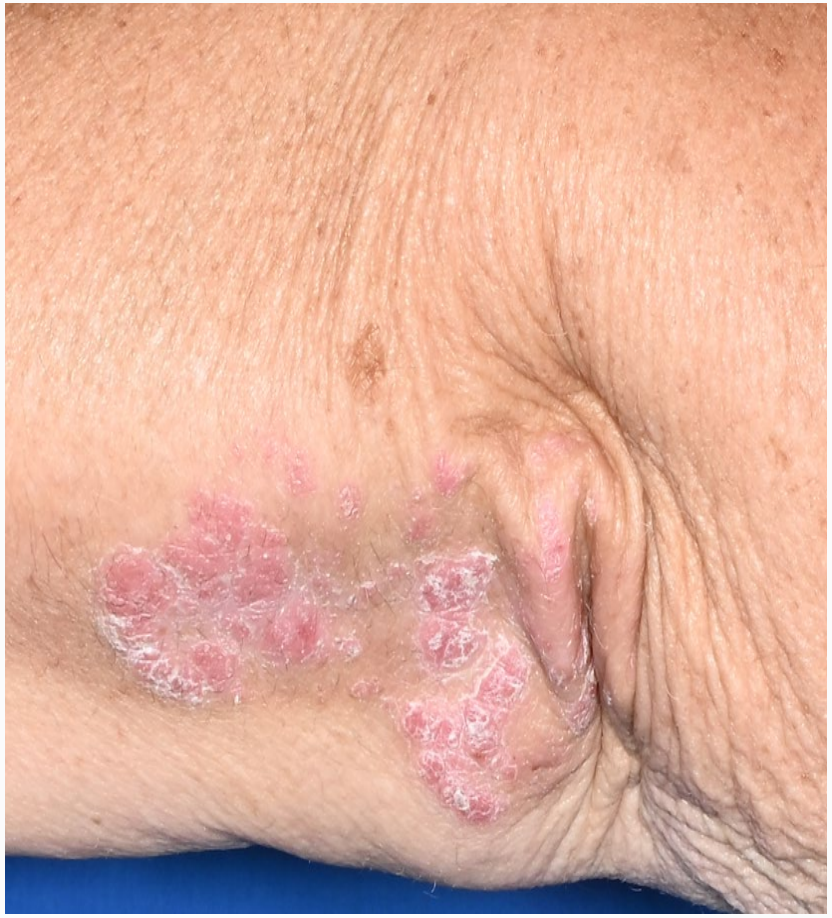
Day 1
(PASI 12.1)



Week 6
(PASI 2.0)



Week 12
(PASI 3.0)



Data Summary

Safety and Tolerability

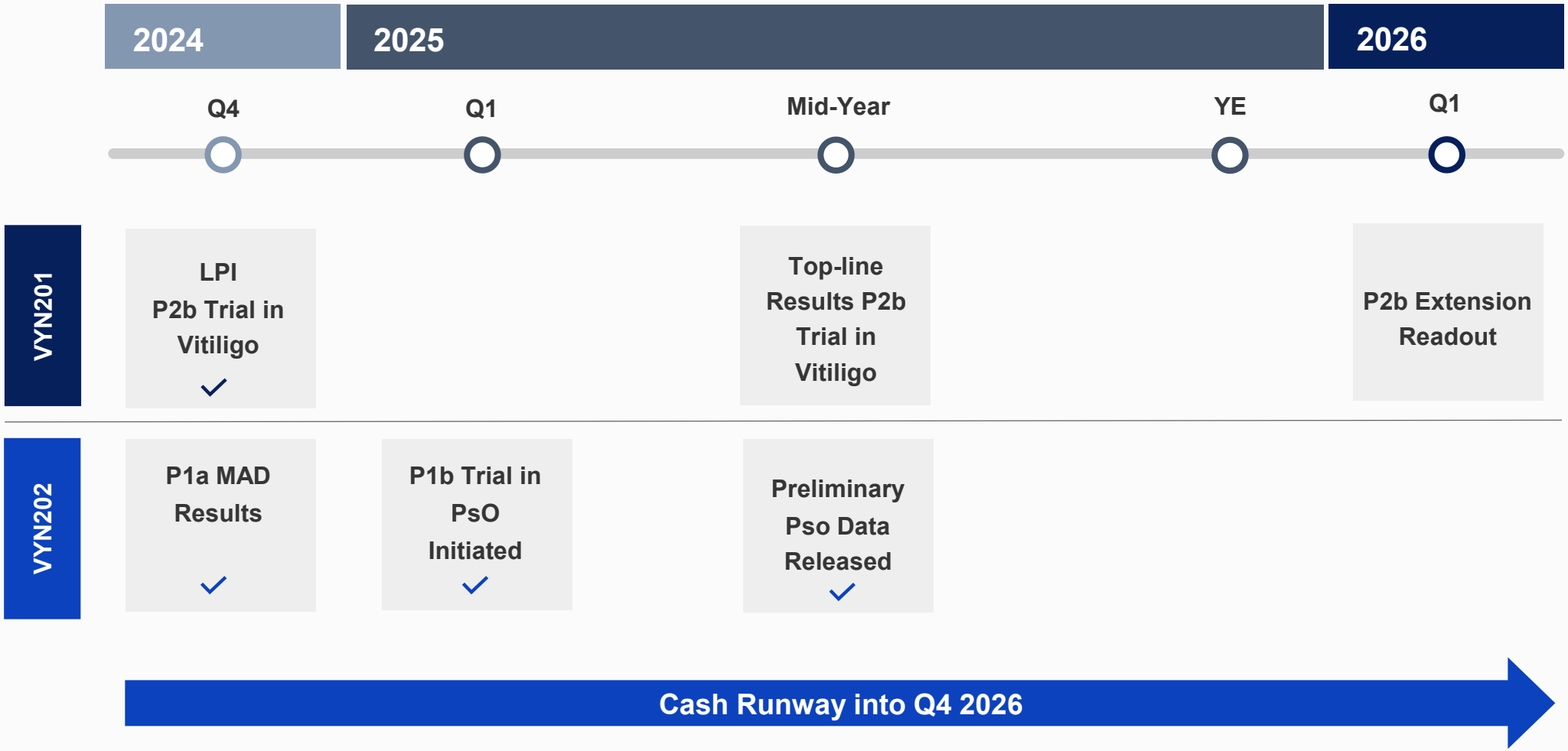
- No TESAEs or discontinuation due to a clinical TEAE
- No treatment interruptions due to a clinical TEAE
- No grades of thrombocytopenia, neutropenia or lymphocytopenia

Exploratory Efficacy

- All subjects receiving VYN202 had an improvement in signs and symptoms of disease, including scalp psoriasis:
  - Improvement in PASI scores ranged from ~27% reduction after 1 week of treatment to ~90% reduction at week 8
- Improvements (reduction) in serum cytokine levels observed in subjects treated with VYN202 for greater than 1 week, including IL17A, IL17F, IL19, and IL22 ranging from -17% to -83%. There was no change in these serum cytokines for the subject receiving placebo.
- Two subjects enrolled co-presented with psoriatic arthritis (n=1 treated with VYN202 0.5 mg; n=1 treated with placebo)
  - Subject treated with VYN202 0.5 mg reported a four-point improvement in joint pain NRS scale by week 2 which corresponded with a -48% reduction in serum c-reactive protein level, a biomarker associated with psoriatic arthritis and other rheumatic diseases.
  - Subject treated with placebo had no improvement in joint pain NRS and no change in serum c-reactive protein levels.

Preliminary data available as of 6/20 and 6/30

Multiple Paths to Potential Value Creation Across BET Inhibitor Programs



Based on current estimates; LPI = Last Patient In

NASDAQ: VYNE

Appendix

VYNE™ THERAPEUTICS

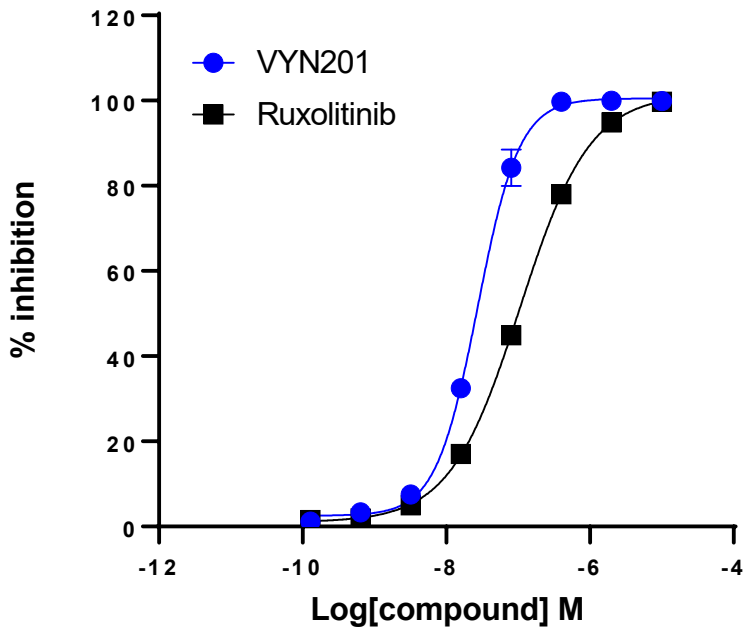
Repibresib (VYN201): Vitiligo

VYNE™ THERAPEUTICS

Pathogenesis of Vitiligo is Primarily Linked to CD8+ T-Cell Proliferation and Hyperactivity

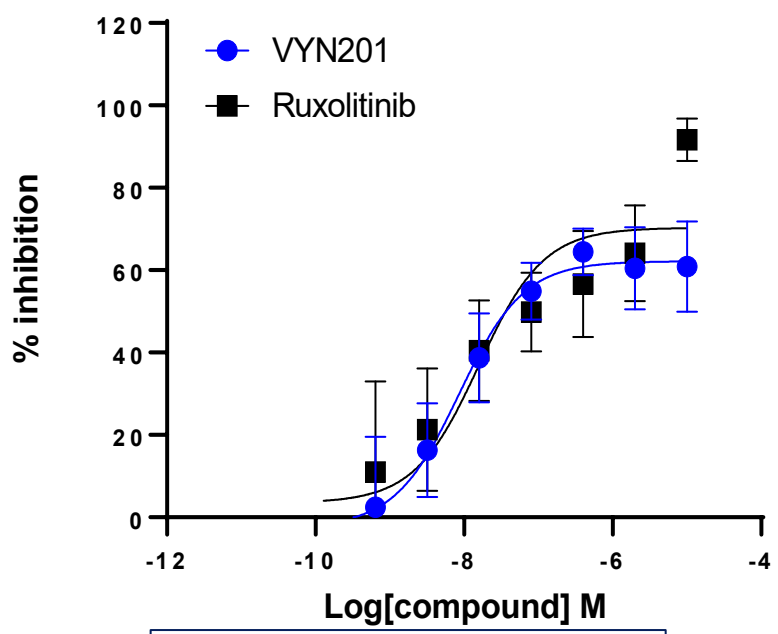
Repibresib (VYN201) has demonstrated marked inhibition of CD8+ t-cell expansion and activity at levels favorable to ruxolitinib

CD8+ T-cell Proliferation



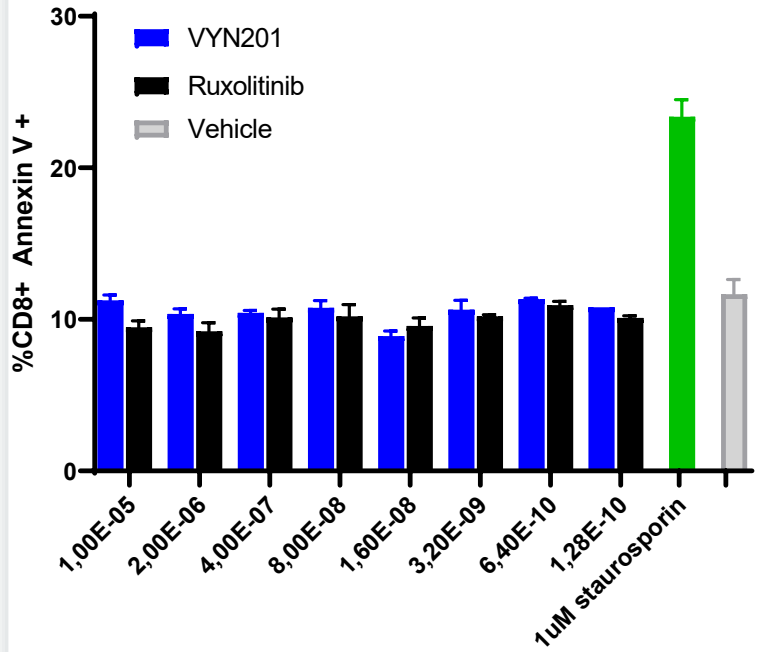
VYN201 mean IC50: 15nM
Ruxolitinib mean IC50: 121nM

CD8+ T-cell Activation Marker IFNγ



VYN201 mean IC50: 8.5nM
Ruxolitinib mean IC50: 15.8nM

CD8+ T-cell Viability



VYN201 is superior to ruxolitinib in inhibiting CD8+ t-cell proliferation

VYN201 IC50 for IFNγ release superior to ruxolitinib

VYN201 does not impart a cytotoxic effect on CD8+ t-cells at levels similar to ruxolitinib

Repibresib (VYN201) P1b Baseline Demographic and Clinical Characteristics

	0.5% Cohort (N=10)		1% Cohort (N=10)		2% Cohort (N=9)		Total (N=29)	
Age - year mean	49.2		53.2		57.0		52.9	
Age group - no. / %	0	0%	0	0%	0	0%	0	0%
12-17	0	0%	0	0%	0	0%	0	0%
18-64	9	90%	8	80%	8	89%	25	86%
>=65	1	10%	2	20%	1	11%	4	14%
Female sex - no. / %	6	60%	7	70%	7	78%	20	69%
Race or ethnic group								
Hispanic or Latino	0	0%	2	20%	7	78%	9	31%
Not Hispanic or Latino	10	100%	8	80%	2	22%	20	69%
Fitzpatrick Skin type - no. / %								
I	0	0%	0	0%	0	0%	0	0%
II	5	50%	4	40%	1	11%	10	34%
III	1	10%	3	30%	3	33%	7	24%
IV	3	30%	2	20%	4	44%	9	31%
V	0	0%	0	0%	1	11%	1	3%
VI	1	10%	1	10%	0	0%	2	7%
F-VASI mean / (min-max)	1.34	(0.54-3.21)	1.14	(0.51-3.36)	0.83	(0.51-1.92)	1.11	(0.51-3.36)
Disease stability - no. / %								
Active / Progressive	10	100%	10	100%	9	100%	29	100%
Stable	0	0%	0	0%	0	0%	0	0%

Demonstrated Favorable Safety & Tolerability Profile in P1b

Adverse Events

- **No** serious adverse events reported
- **No** treatment related discontinuations
- **All** TEAEs classified as **mild (>70%) or moderate**; except for 2 severe events of application site pain reported for 1 subject in 2% cohort which resolved
- **No** dose/exposure-dependent increases in AEs
- **No** significant alterations in clinical safety lab parameters, with no impact on platelet counts

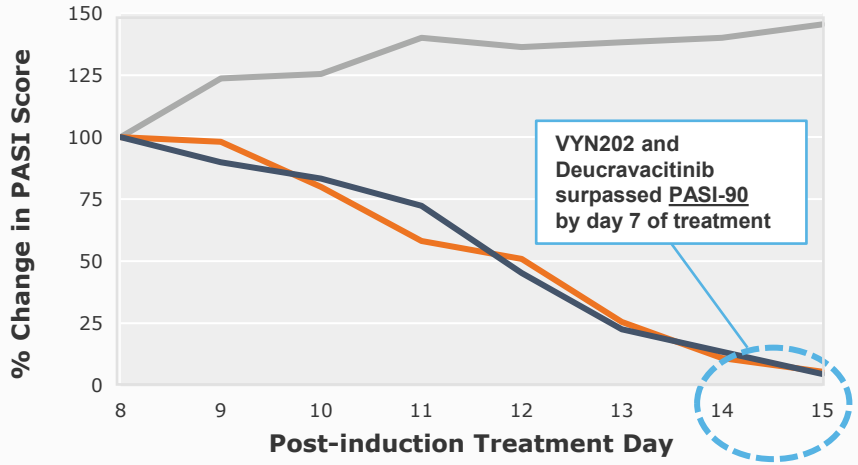
Local Skin Tolerability

Assessment	Mean Score Range 0 (None) to 3 (Severe)
Burning/Stinging	0.26
Scaling	0.15
Dryness	0.22
Pruritus	0.14
Erythema	0.29
Hyperpigmentation	0.10

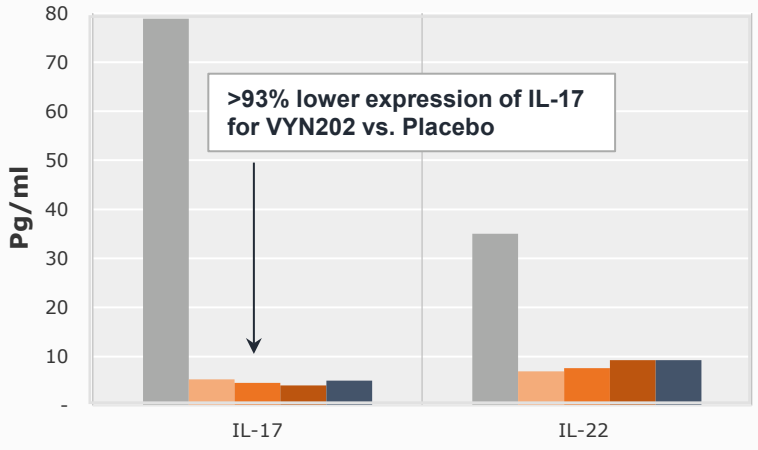
VYN202: Preclinical Efficacy Models

VYNE™ THERAPEUTICS

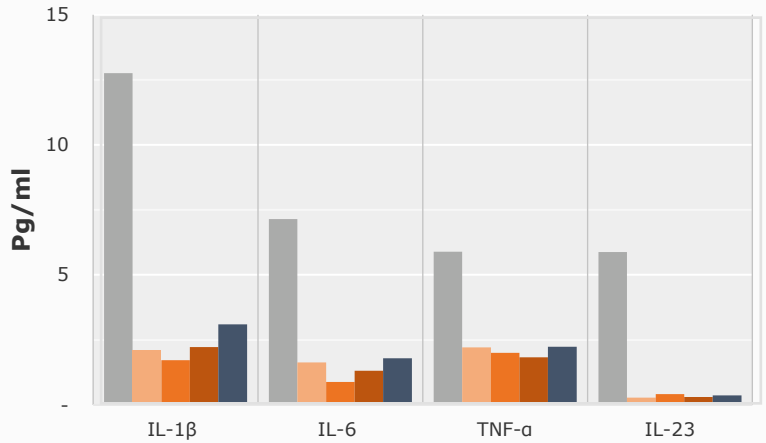
VYN202: Clinical and Biomarker Effects Comparable to Deucravacitinib in Preclinical *in vivo* Model of Psoriasis



Day 15 After 7 days of treatment



>93% lower expression of IL-17 in blood at all VYN202 doses compared to placebo



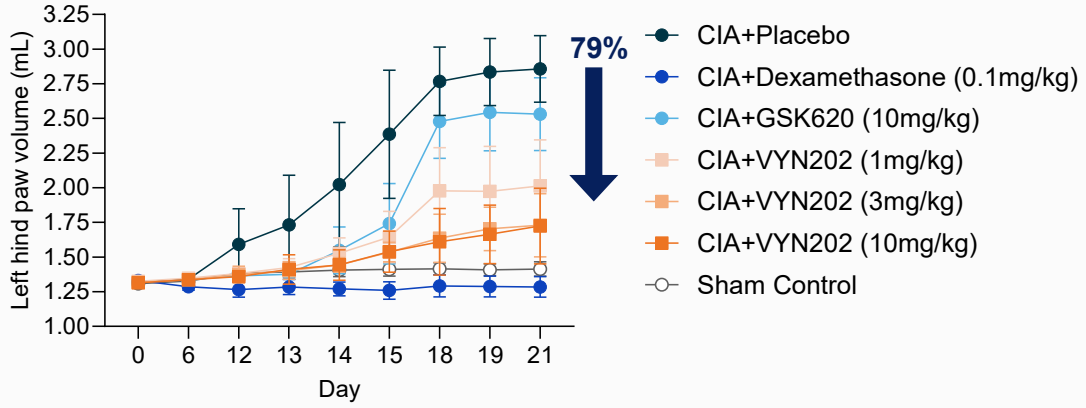
Marked reduction of other disease related Th17 and Th1 cytokines in blood

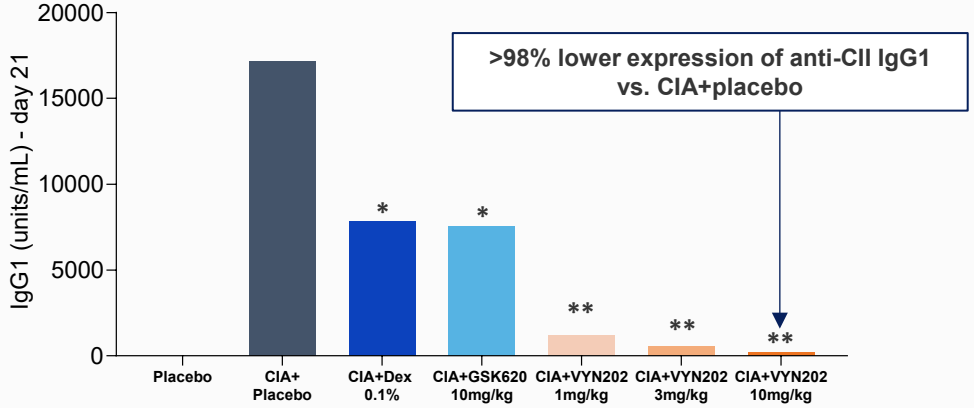
1Sotyktu® (deucravacitinib) was approved in the U.S. in September 2022.; PASI-90 = 90% improvement from baseline in PASI score;
Dorsal depilated BALB-C mice were dosed for 14 days with topical IMI cream (Day 1-7: induction phase, Day 8-14: treatment phase); IMI = imiquimod

VYN202: Anti-Arthritic Effect and Decreased Antibody Levels Demonstrated in Preclinical Models of Arthritis

Collagen-Induced Arthritis Model

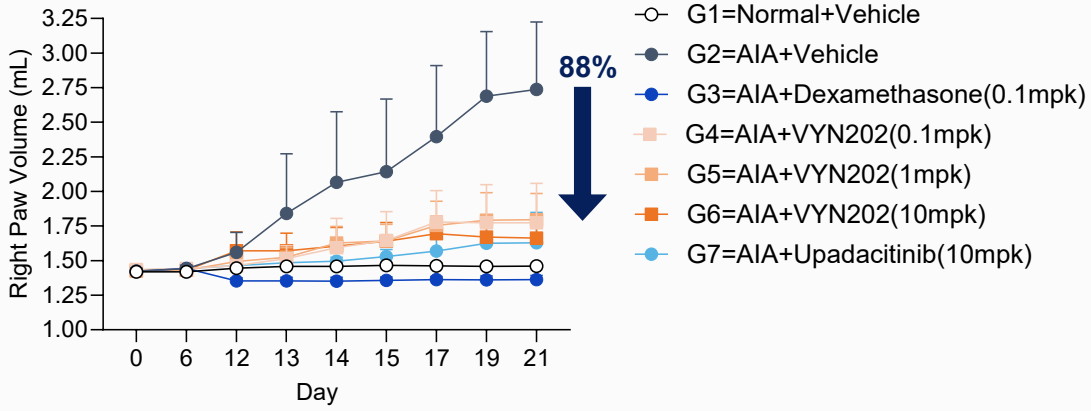
- VYN202's increased potency and selectivity led to improved outcomes vs. early generation BET inhibitor, GSK620
- VYN202 treatment resulted in dose-dependent reduction in severity of histopathology scores; Statistically superior to Placebo and GSK620

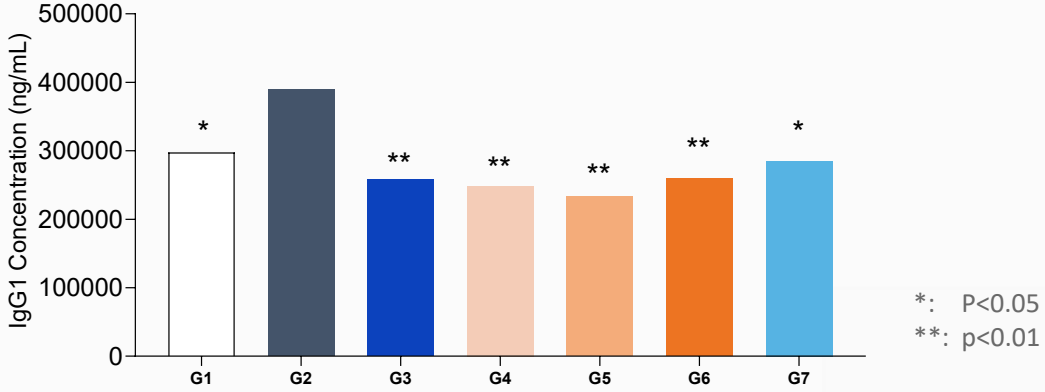




Adjuvant-Induced Arthritis Model

- Comparable effect on paw volume and IgG1 expression to Upadacitinib
- Histopathology scores showed significant effect on preventing ankle inflammation vs. control for VYN202 10mpk (67% reduction vs. control) and Upadacitinib 10mpk (56% reduction vs. control)



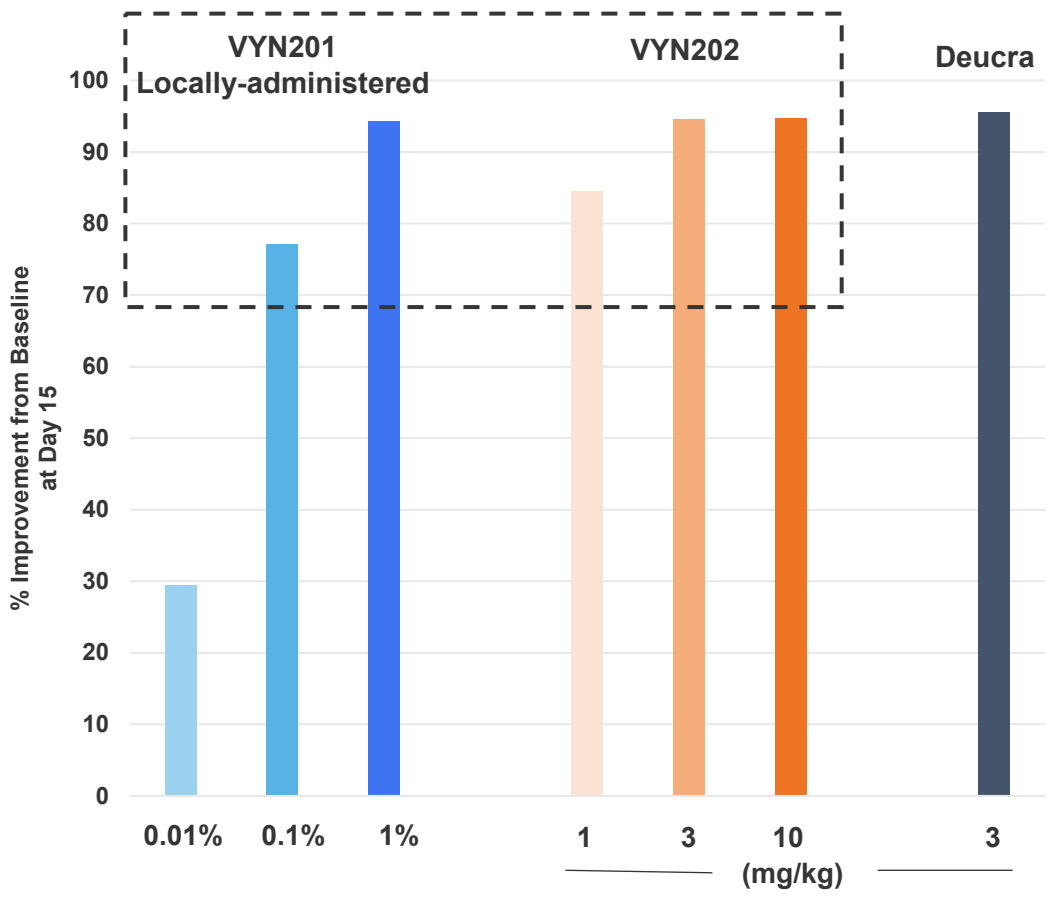


1Histopathology data on file

VYN202 Results Show Strong Correlation with VYN201 Results

Reinforcing BET potential and role of BD2 inhibition in treatment of I&I diseases

Psoriasis Model



Arthritis Model (CIA)