VYNE™ THERAPEUTICS

Corporate Presentation

September 2024

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 autoimmune diseases: Addressing the complex signaling of immuno-inflammatory diseases by disrupting inflammatory gene transcription in T cells
- Potential across broad range of immune-mediated diseases representing multi-billion-dollar opportunities

Clinical Stage Pipeline

- VYN201: Phase 1b PoC data in vitiligo suggest VYN201 has the potential to be category leader
- VYN202: Supported by robust preclinical data across multiple diverse models of autoimmune disease, Phase 1a SAD/MAD initiated in Q2 2024

Potential for Multiple Clinical Catalysts

- VYN201: Phase 2b trial initiated in Q2 2024, with top-line results anticipated in mid-2025
- VYN202: Phase 1a SAD & MAD read-outs anticipated in Q3 2024 (complete) and Q4 2024, respectively
  - (2) Phase 1b PoC studies in plaque psoriasis and rheumatoid arthritis planned, with top-line results anticipated in 2H 2025

Experienced Team & Strong Balance Sheet

- Seasoned leadership team with demonstrated track record of progressing programs through regulatory approval
- Balance sheet expected to fund key clinical milestones for VYN201 and VYN202 through end of 2025

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	IND-Enabling	Phase 1	Phase 2		
InhiBET™ Platform - Library of NCE BET Inhibitors for Any Indication Worldwide								
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	Moderate-to-Severe Plaque Psoriasis	Oral					• Q2 2024: P1a SAD/MAD initiated • Q3 2024: P1a SAD completed • Q4 2024: TLR P1a MAD	Worldwide
	Moderate-to-Severe Rheumatoid Arthritis							
Ongoing evaluation for other autoimmune and fibro-inflammatory diseases								

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

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InhiBET™ BET Inhibitor Platform

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

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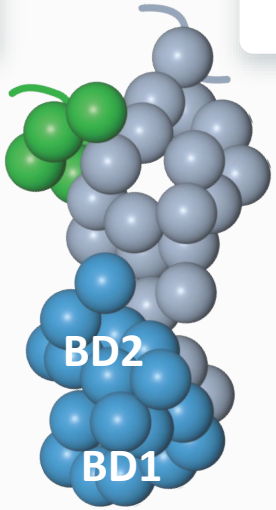
VYNE's Drug Design Strategy

Optimize benefit/risk profile of BET inhibitors to target autoimmune diseases

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

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

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

VYN201: Vitiligo

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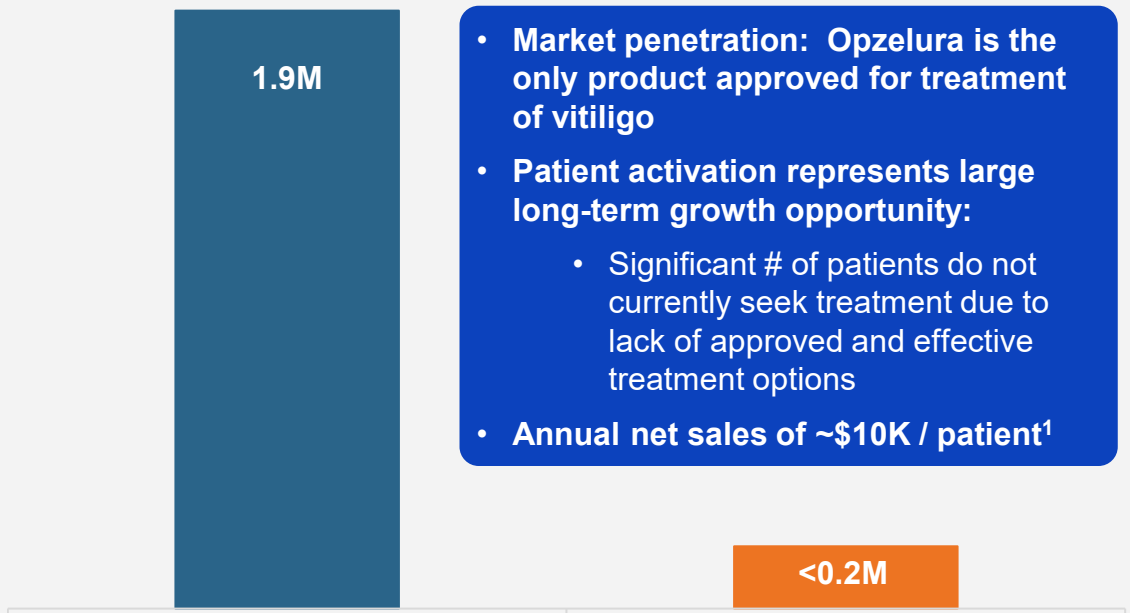
Vitiligo Represents a Large and Growing Market Opportunity

Addressable Market : a Significant Unmet Need



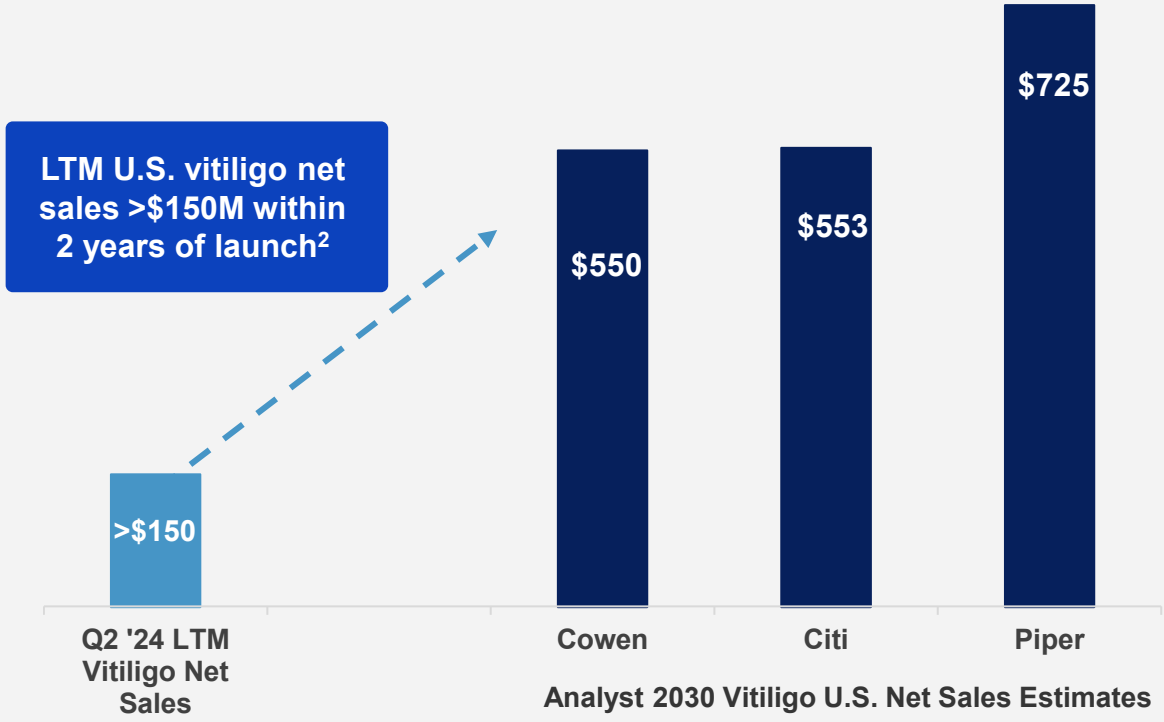
- **Market penetration: Opzelura is the only product approved for treatment of vitiligo**
- **Patient activation represents large long-term growth opportunity:**
  - Significant # of patients do not currently seek treatment due to lack of approved and effective treatment options
- **Annual net sales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

Opzelura® (ruxolitinib) cream 1.5%

$ in millions

Est. 0.3M to 0.45M patients seeking treatment

LTM U.S. vitiligo net sales >$150M within 2 years of launch[2]



Analyst 2030 Vitiligo U.S. Net Sales Estimates

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

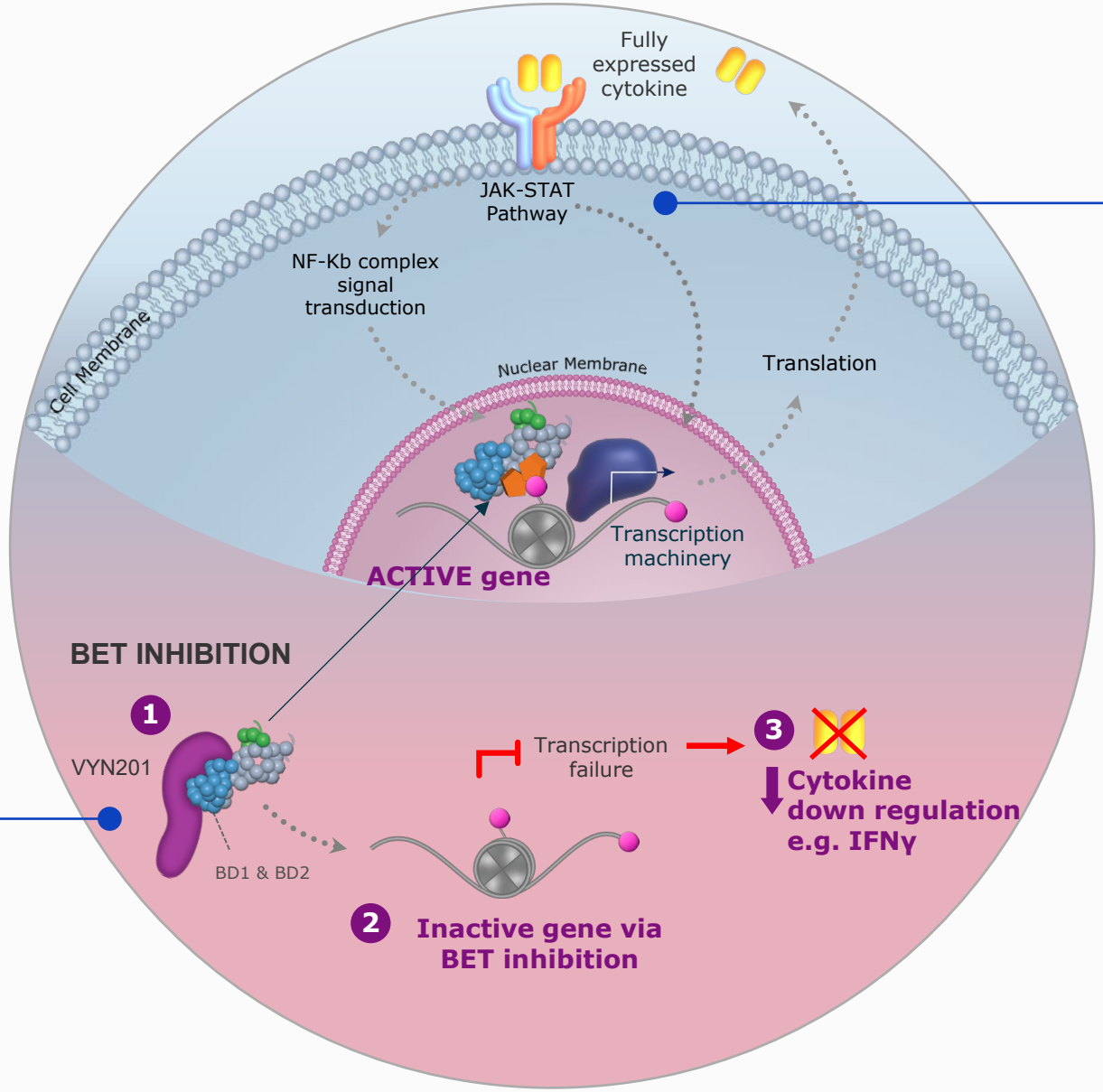
Source: Gandhi et al. JAMA Dermatol. 2022;158(1):43-50; Kruger. 2012;51(10):1206-1212; Rangu. J Clin Dermatol Ther. 2021;7:070; Pandya. AAD 2023 Presentation; Incyte Corporate Pres. Aug. 2023; TD Cowen research dated Sept. 2023; Piper research dated Jan. 2023; Citi research dated July 2023

1. Opzelura estimated pricing: $2k per 60g tube*10 tubes per patient per year less GTN discount of 50% per Incyte mgmt.; 2. Estimated: Q2'24 LTM net sales $392M with vitiligo representing ~40% of TRx per Incyte mgmt.

BET Inhibition – A Differentiated Treatment Strategy for Non-Segmental Vitiligo

BET Inhibition (VYN201)

- BET proteins recognize (“read”) acetylated lysine on the termini of histones that protrude from chromatin.
- **BET inhibition prevents transcriptional processing, leading to signal transduction termination.**



JAK-STAT pathway Opzelura® (ruxolitinib)

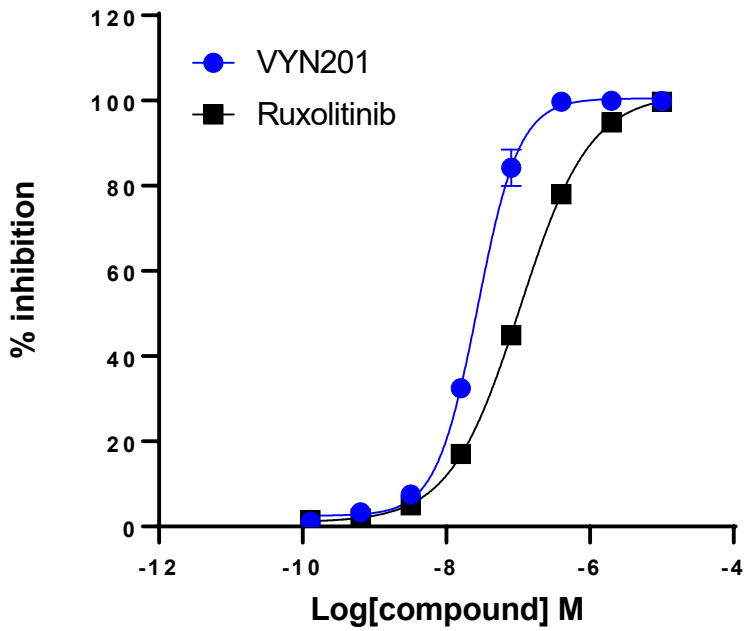
- JAK activation phosphorylates receptors that form docking sites for STAT
- **JAK inhibition prevents STAT signal transduction into the nucleus.**

Adapted from Gonzalez-Gay et al, Autoimmunity Rev, (2020) 19: 102429 and Rusinol and Puig, Int J Mol Sci, (2023) 24: 3391

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

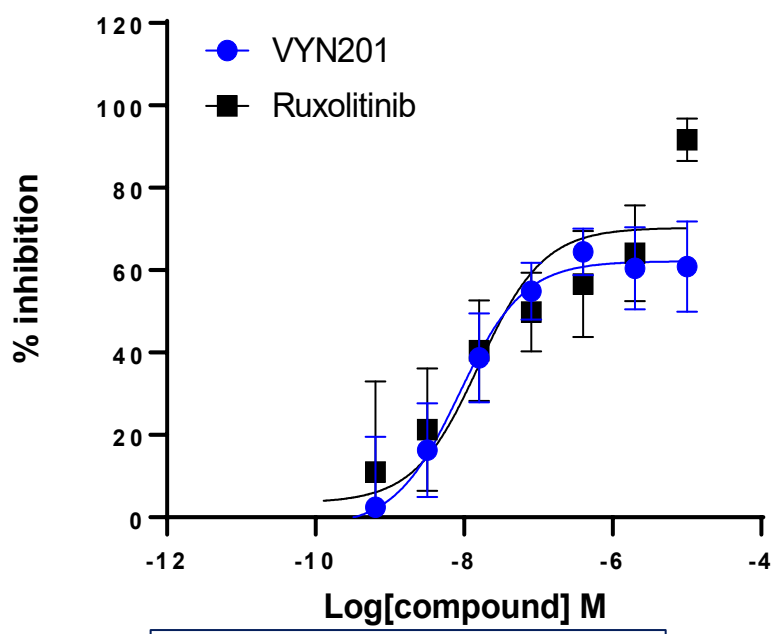
VYN201 has demonstrated marked inhibition of CD8+ t-cell expansion and activity at levels favorable to ruxolitinib

CD8+ T-cell Proliferation



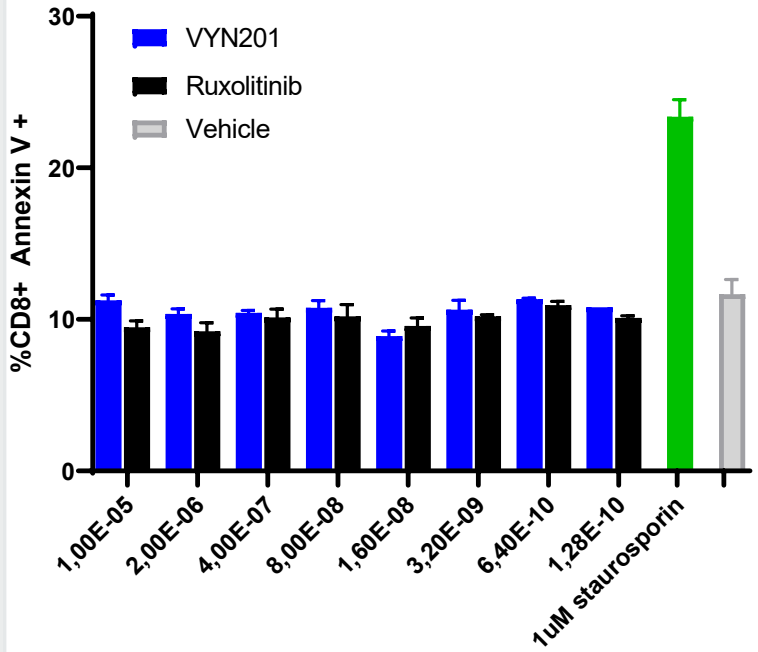
VYN201 mean IC50: 15nM
Ruxolitinib mean IC50: 121nM

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

VYN201: Phase 1 Proof-of-Concept

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VYN201: Phase 1b Study in Active Vitiligo Patients

Study Design

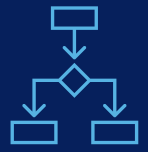
Treatment on the face and target lesion on trunk of active vitiligo patients for up to 16 weeks of QD treatment

- **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

Vitiligo Disease Activity within PoC Study Designs

Patient Population and Asset Development Status

	Disease Activity	Status
VYN201 P1b *(VYNE)*	• **Active Only**	• PoC achieved • Phase 1b completed
Litfulo® (ritlecitinib) P2b[1] JAK3/TEC kinase inhibitor *(Pfizer)*	• **Active Only**	• Phase 3 studies evaluating 50 mg QD dose in active & stable disease ongoing
Opzelura® (ruxolitinib) P2b[2] JAK1/JAK2 inhibitor *(Incyte)*	• **Active & Stable**	• 1.5% BID dose approved in the U.S. (July 2022) and EU (April 2023)
Povorcitinib P2b[3] JAK1 inhibitor *(Incyte)*	• **Active & Stable**	• Phase 3 studies ongoing
Rinvoq® (upadacitinib) P2b[4] JAK1/JAK2 inhibitor *(AbbVie)*	• **Active & Stable**	• Phase 3 studies ongoing

VYNE is currently enrolling patients with <u>active and stable</u> disease in P2b study

Patients with Active Disease Will Continue to Depigment in Areas that Show High Activity without Therapy[5]

Fig 1:
Vitiligo of the hand with confetti-like depigmentation

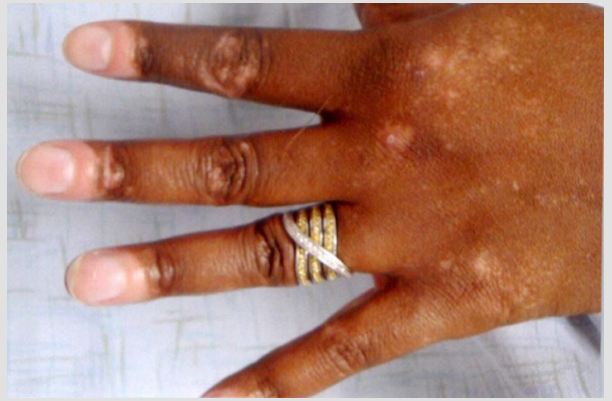
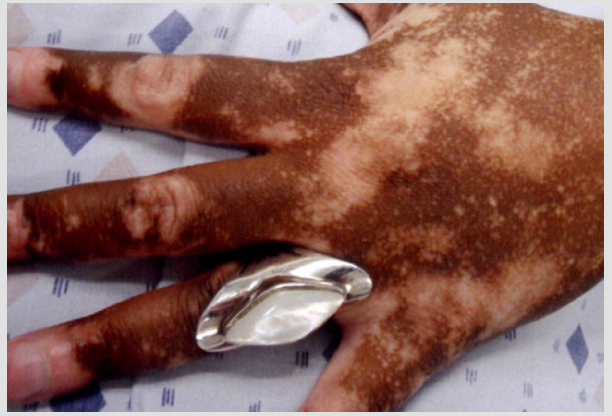


Fig 2:
16 weeks later
Showing extension of depigmentation and new areas of confetti-like depigmentation

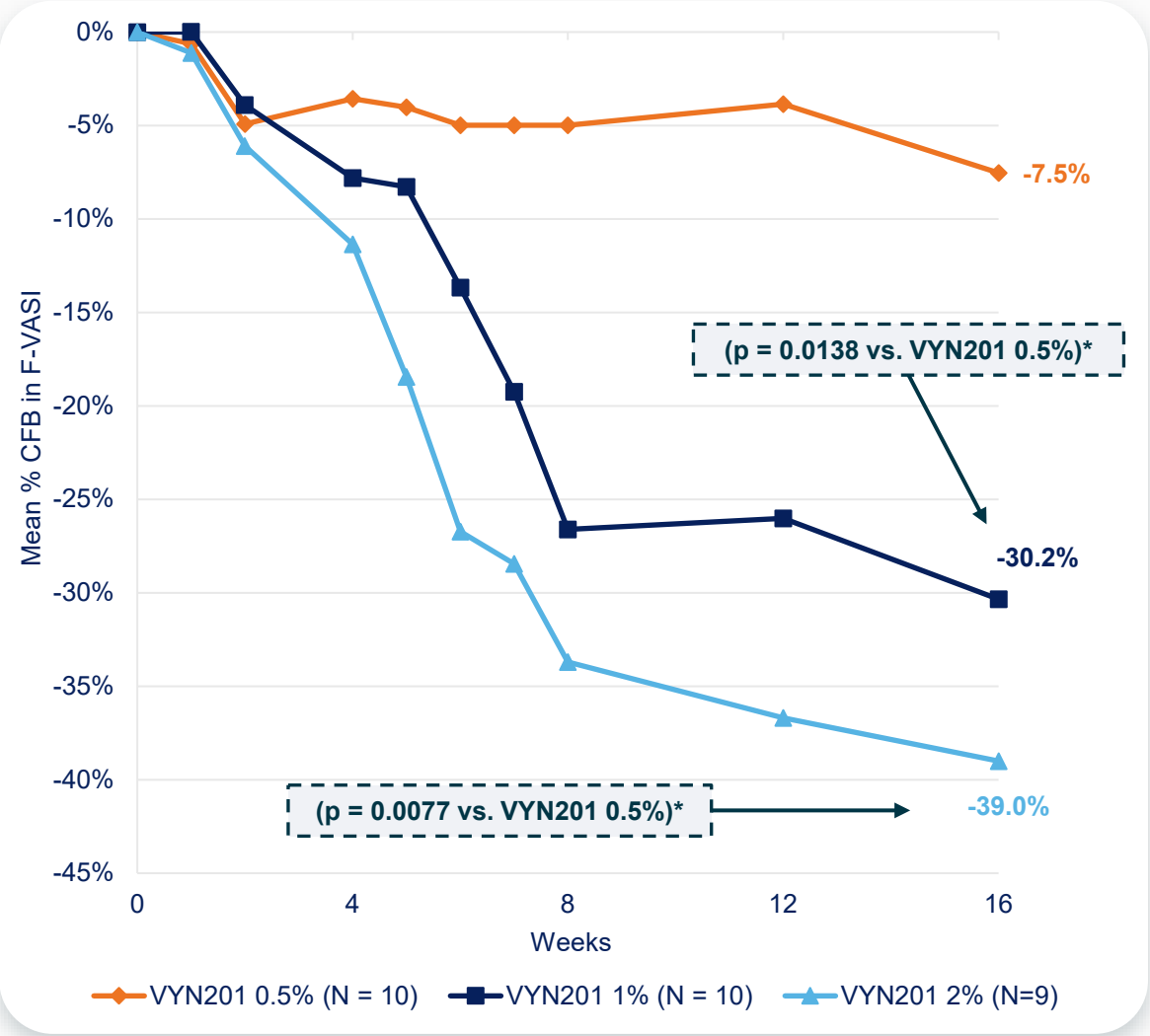


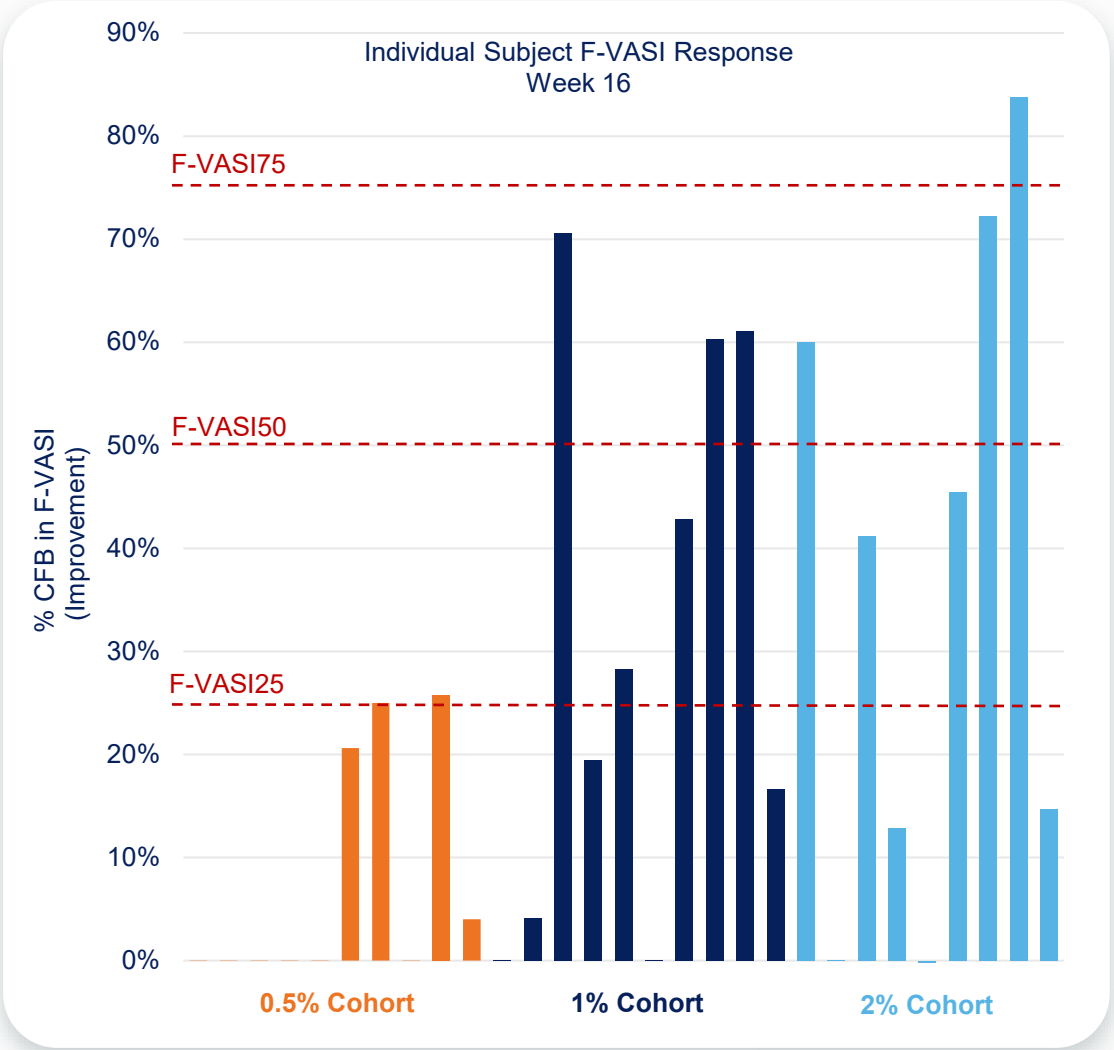
Physicians expect patients with active disease to be more difficult to treat

Source: Data on file; 1. NCT03715829; 2. NCT03099304; 3. NCT04818346; 4. NCT04927975; 5. Sosa et al, J Am Acad Dermatol 2015

Promising Onset of Action and F-VASI Response

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

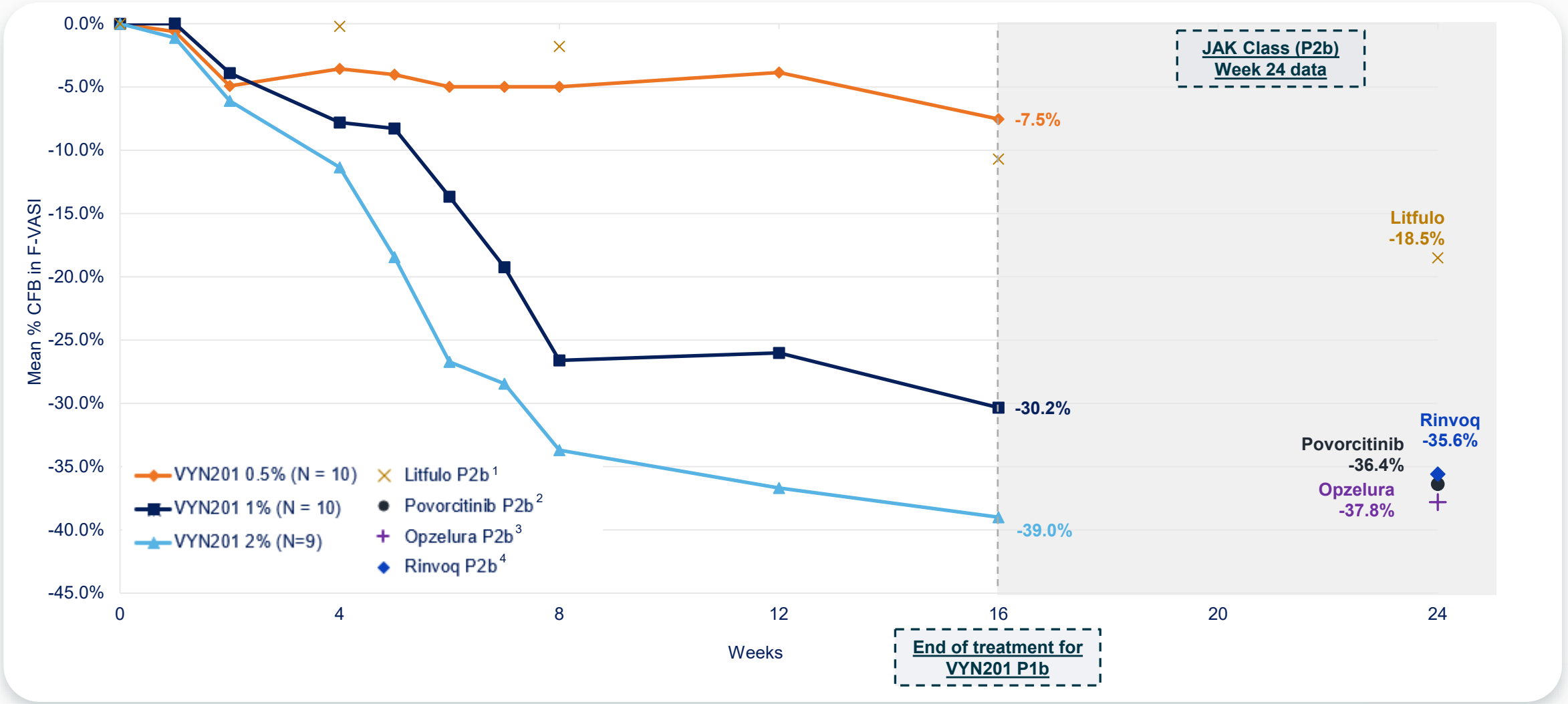




*% CFB T-test based on latest observed case (LOCF)

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

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);

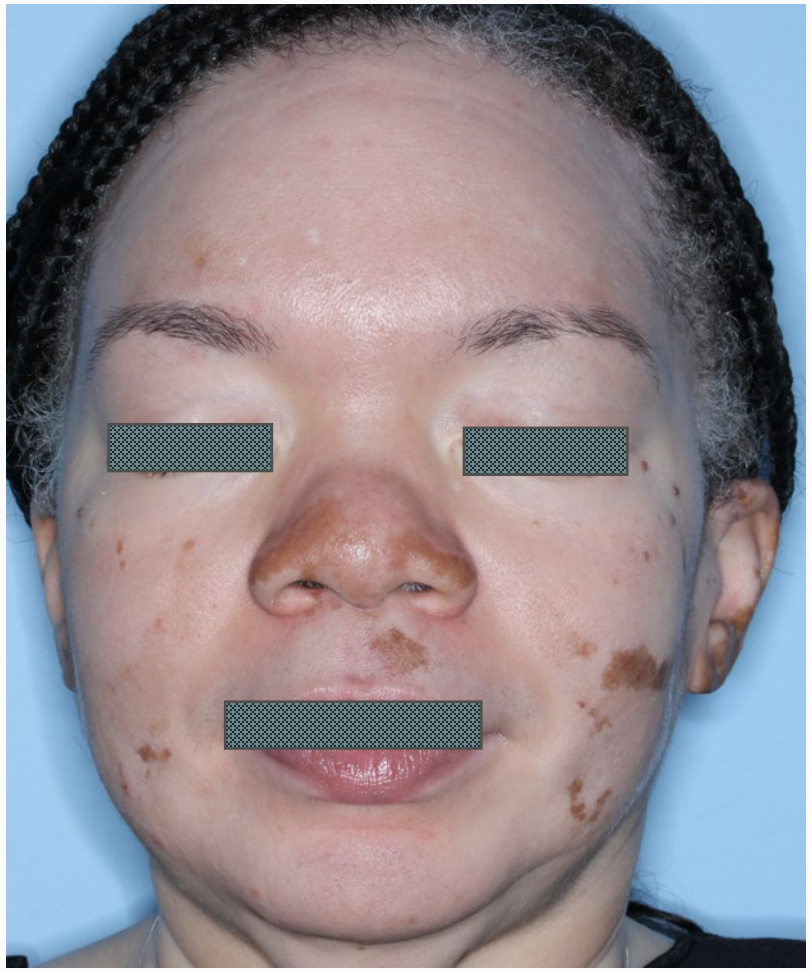
Preclinical & Clinical Data Highlight Potential for Differentiated Product Profile

Characteristic	VYN201		Opzelura (Ruxolitinib) Cream 1.5%	Litfulo (Ritlecitinib) 50mg[1]	Povorcitinib 45mg[2]
	1%	2%			
Novel MOA / JAK Class Alternative	✓		✗	✗	✗
Targeted Dosing Posology	QD		BID	QD	QD
Rapid Onset of Action	✓		Moderate	✗	Moderate
Efficacy, % CFB F-VASI, Week 16	**100% active disease study**		**Active & stable disease study** P2b: -37.8 (Week 24)[3]	**100% active disease study** -1.8 (Week 8) -18.5 (Week 24)	**Active & stable disease study** -36.4 (Week 24)
	-30.2	-39.0			
Efficacy, % F-VASI50, Week 12[5]	20.0	33.3	P2b: 21.2[3] P3: 29.2[4]	0.0 (Week 8) 15.4 (Week 24)	25.0
Potential to Upregulate WNT Pathway[6]	✓		✗	✗	✗
Safety Precaution	-		✗ "Black Box"	✗ "Black Box"	✗ Expect "Black Box"
Systemic Exposure	Low (Cmax <1 nM)		Cmax/AUC: 449nM / 3215nM	-	-

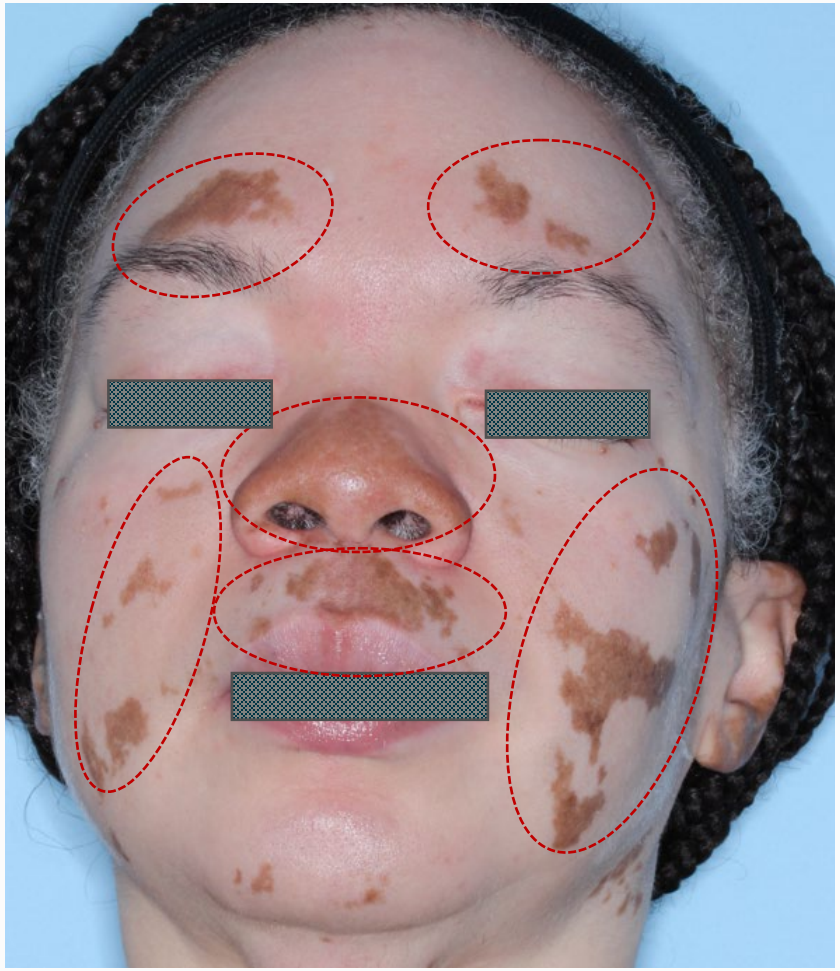
Data is not based on Head-to-Head comparisons
Source: Clinicaltrials.gov; Data on file 1.NCT03715829 2. NCT04818346; 3. NCT03099304; 4. Pooled analysis TRuE-V1 and TRuEV2 Incyte Corporate Presentation dated July 19, 2022; 5. Week 16 data for JAK class not available; 6. Based on preclinical data

Phase 1b Select Images

Subject with near-complete depigmentation (High FVASI)



Baseline

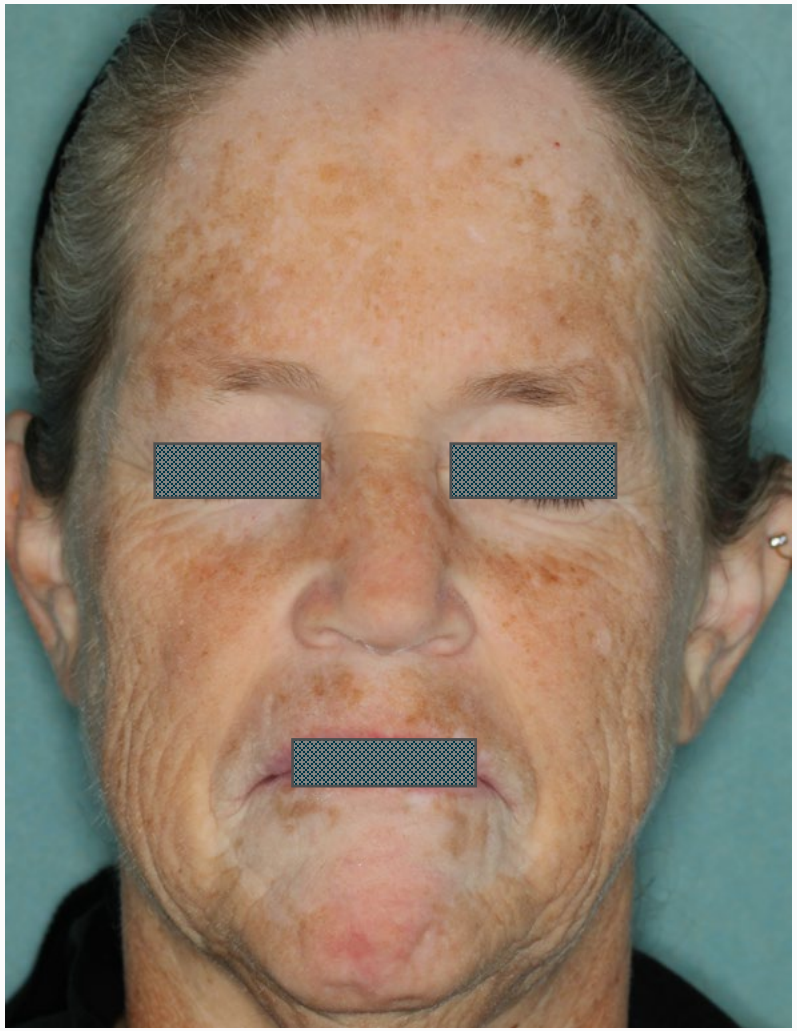


Week 16

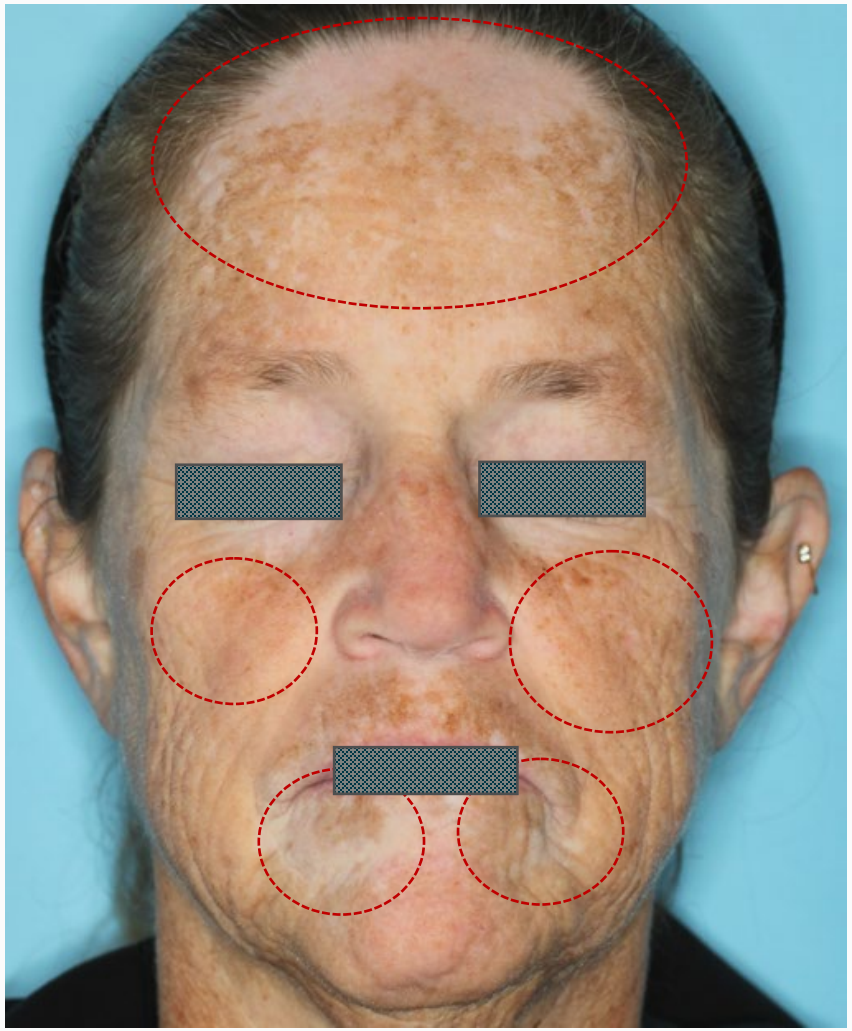
(0.5% cohort, Fitzpatrick skin type: 5)

Phase 1b Select Images

Subject with significant repigmentation response



Baseline



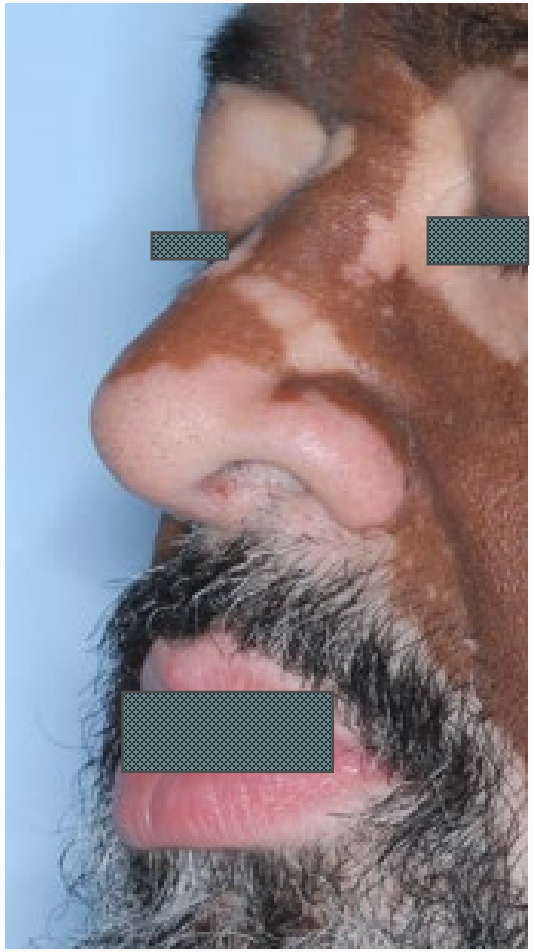
Week 16

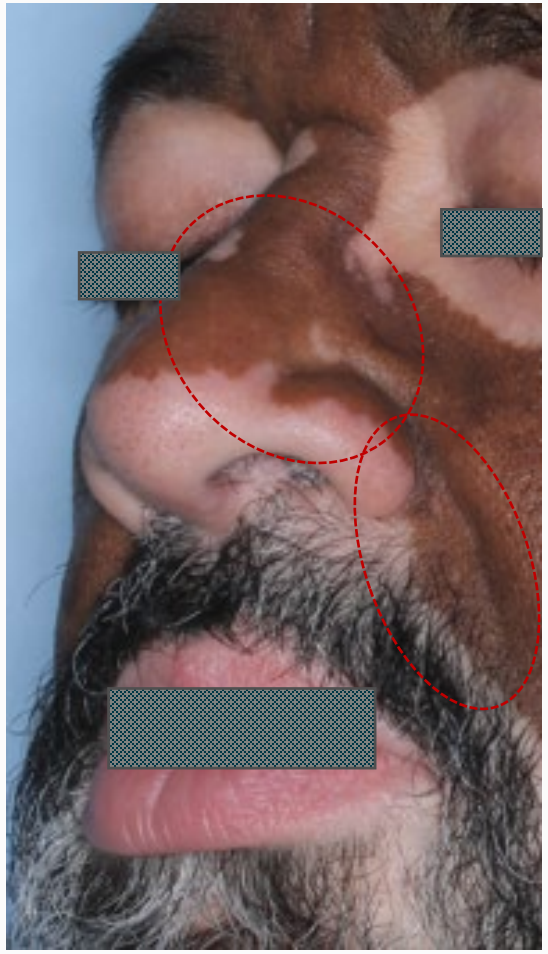
(2.0% cohort, Fitzpatrick skin type: 2)

Phase 1b Select Images

Subject examples with marked active disease

Confetti-like depigmentation presentation

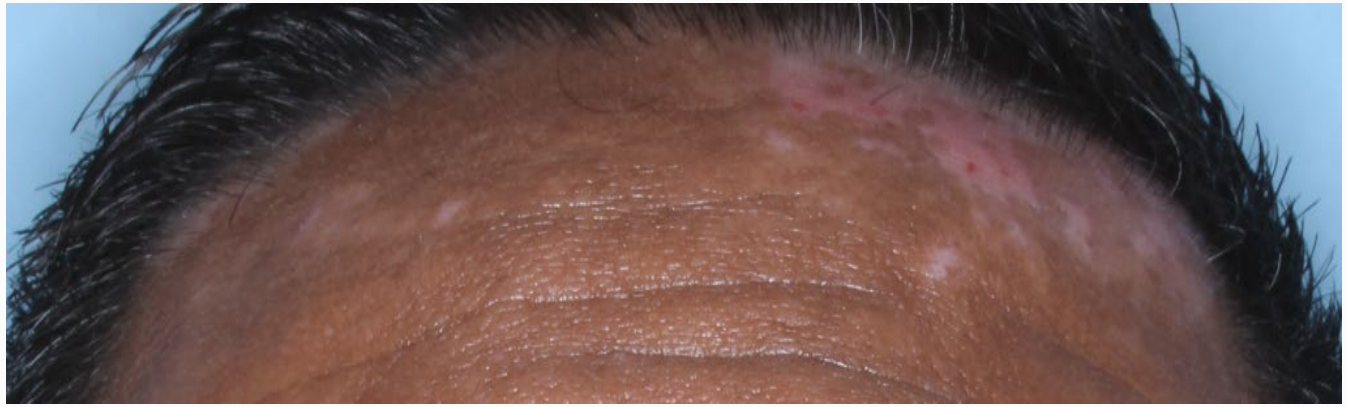




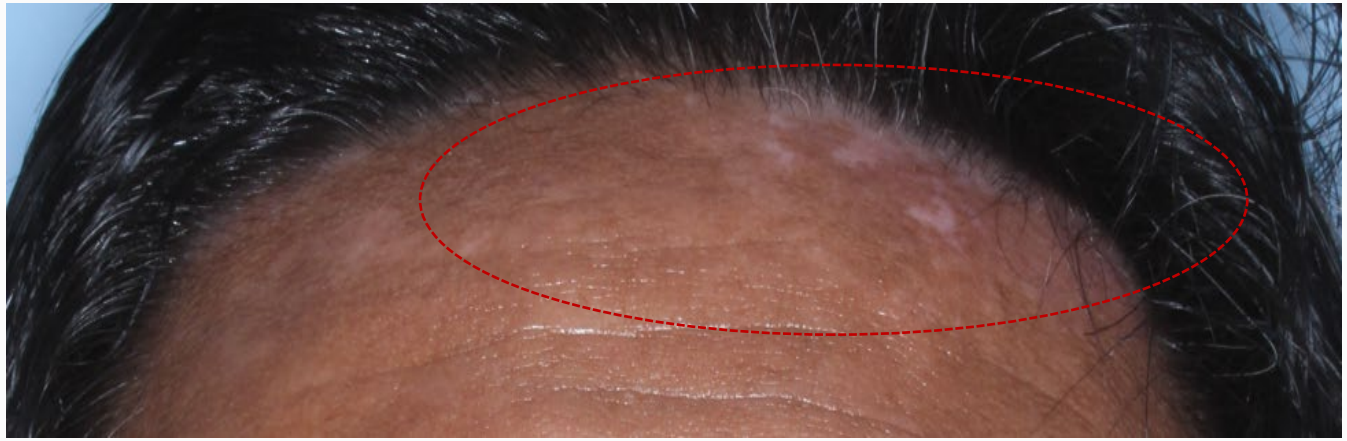
Baseline Week 16

(1.0% cohort, Fitzpatrick skin type: 6)

Inflamed vitiligo presentation



Baseline



Week 16

(2.0% cohort, Fitzpatrick skin type: 5)

Key Takeaways from VYN201 Phase 1b Results

PoC Achieved

- Significant clinical response shown with rapid onset of action
- Clear evidence of dose response

- Efficacy data suggest potential to be category leader
- Favorable efficacy results and onset of action compared with the JAK competitive landscape in a more difficult to treat patient population (active disease vs. stable disease)

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

- Believed to be first clinical demonstration of BET inhibitor’s effect in autoimmune disease[1]

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

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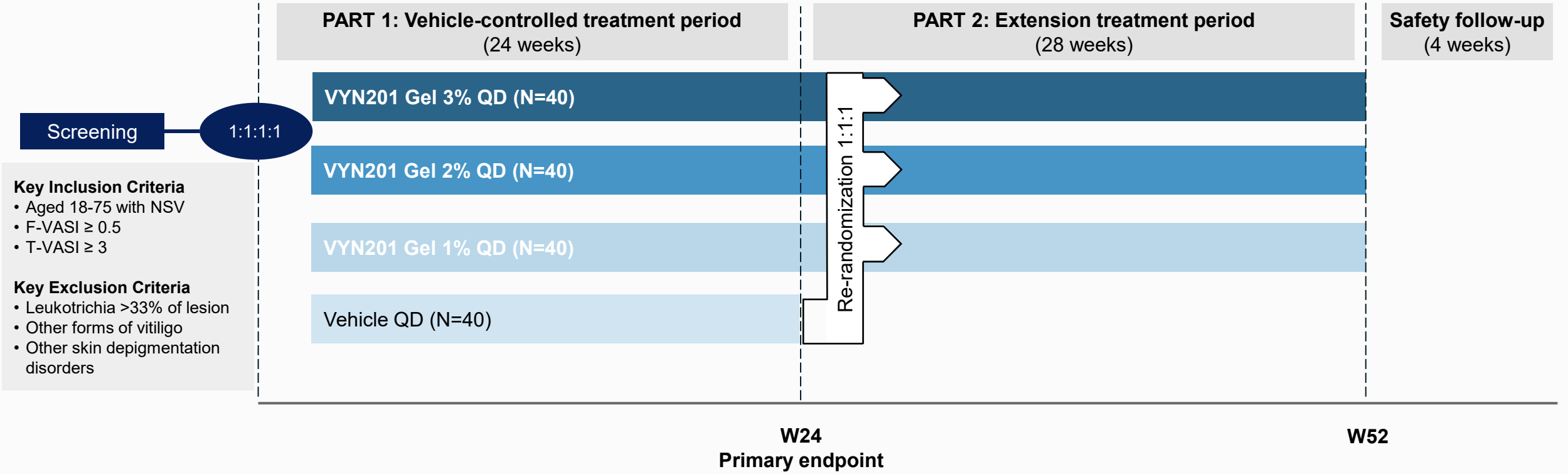
VYN201 Phase 2b in Non-Segmental Vitiligo (NSV)

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

N = ~160 subjects with NSV (active and stable disease)



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 autoimmune diseases

VYN201
Pan-BD BET Inhibitor

Maximize local effect & minimize systemic exposure

- Tissue targeted administration routes & formulations
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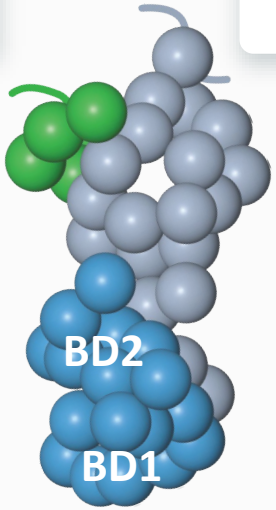

VYN202
BD2-Selective BET Inhibitor

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

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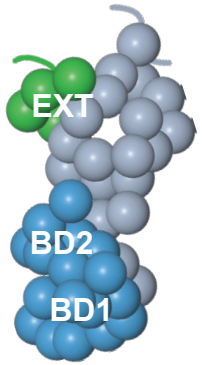
Maximizing On-target Potency vs. BD2 and Minimizing Affinity to BD1 May Be The Key to Optimizing the Benefit/Risk Profile of BET Inhibitors for Autoimmune Diseases

VYN202 is believed to be the most potent and BD2-selective BET Inhibitor in 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

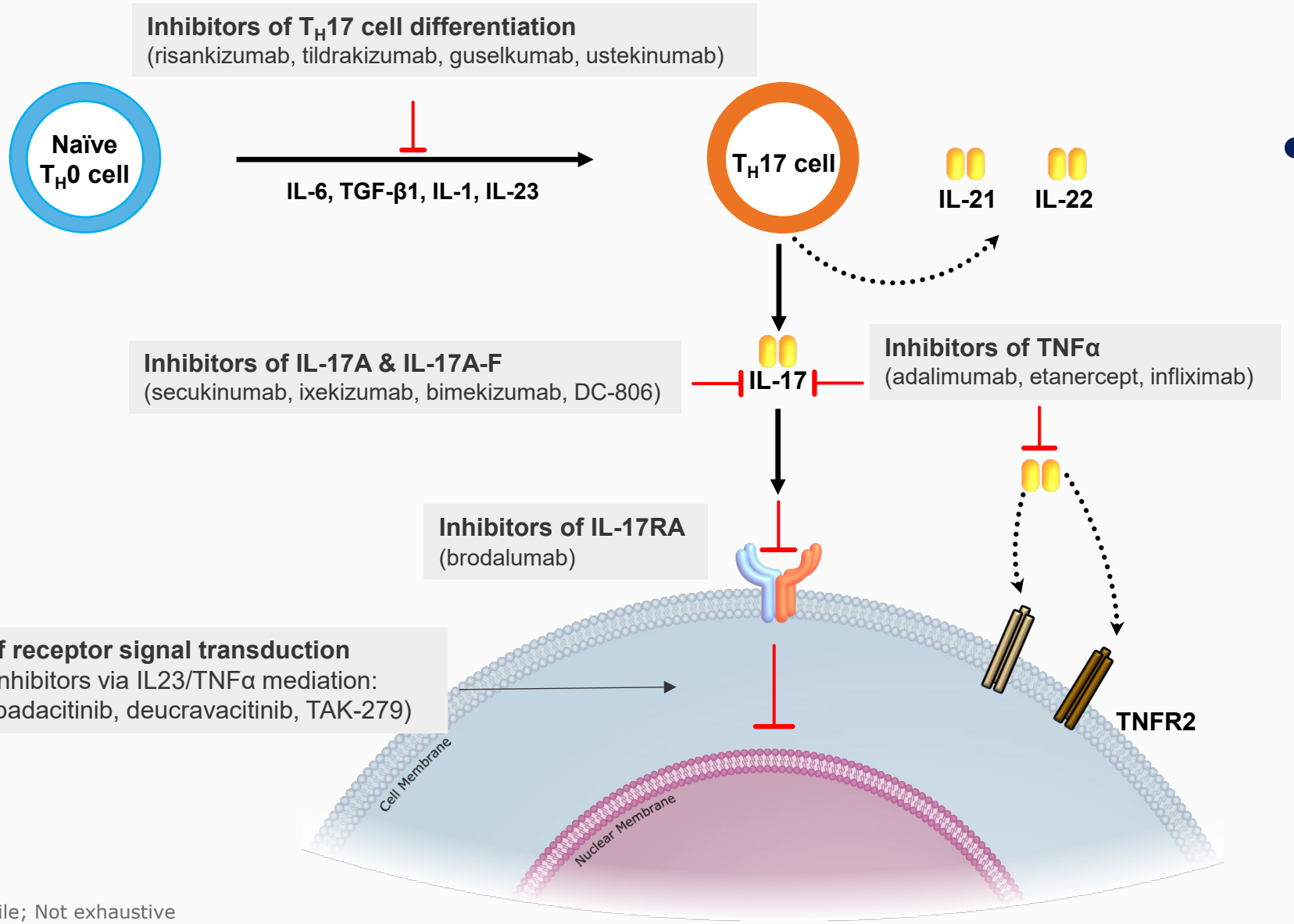
BD1 regulates "housekeeping" gene activity

Compound ID	Potency vs. BD2* (nM)	Selectivity** (BD1/BD2)
VYN202 (VYNE)	**<**	**>>>>**
NUV-868 (Nuvation)[2]	2	1,460x (FRET)
ABBV-744 (AbbVie)[3]	28	753x (FRET)
GSK620 (GSK)[4]	79	220x
Pelabresib (NVS/MOR)[2]	17	5x (FRET)
ABBV-075[3]	13	2.6x
MK-8628/OTX-015[5]	26	1.5x
BI-894999[6]	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. Wang et al 2017 6. Kraut et al 2018; Data on file

Strategies to Control Dysregulated T_H17 Immune Cell Activity



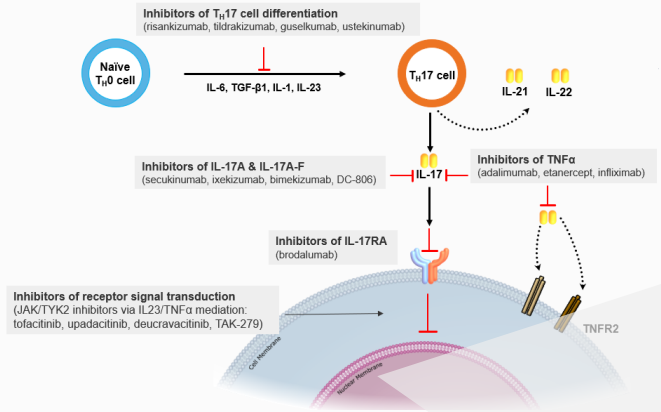
Existing strategies target:

- Extracellular cytokines
- Cytokine receptor inhibition or
- Inhibition of trans-cellular inflammatory signal propagation

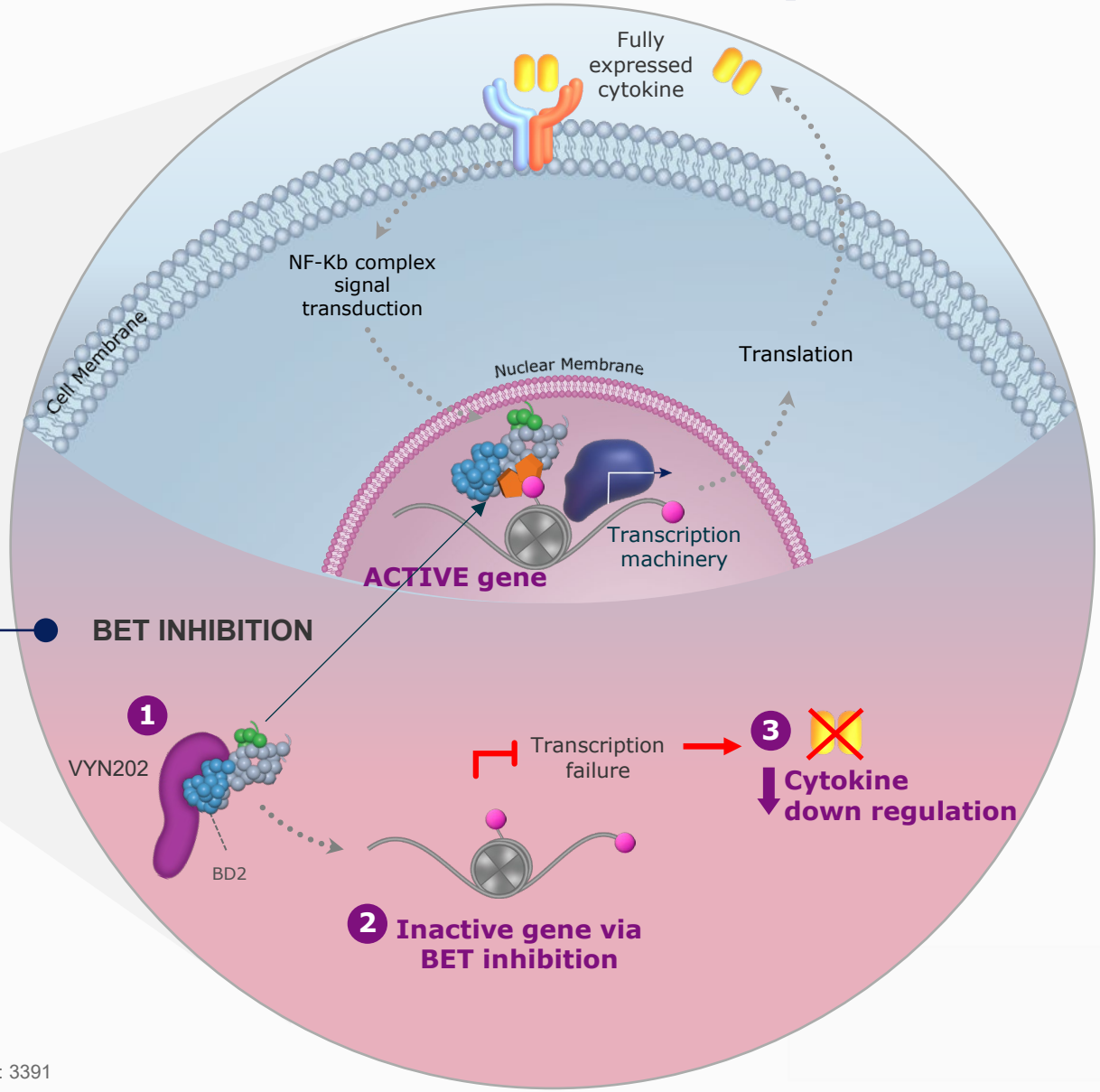
Data on file; Not exhaustive

VYNE™ THERAPEUTICS

BET Inhibitors Disrupt Inflammatory Gene Transcription in T Cells to Directly Address the Complex Signaling of Immuno- & Fibro-inflammatory Diseases



Clinical PoC of BET inhibition in I&I disease demonstrated in VYN201 P1b vitiligo trial

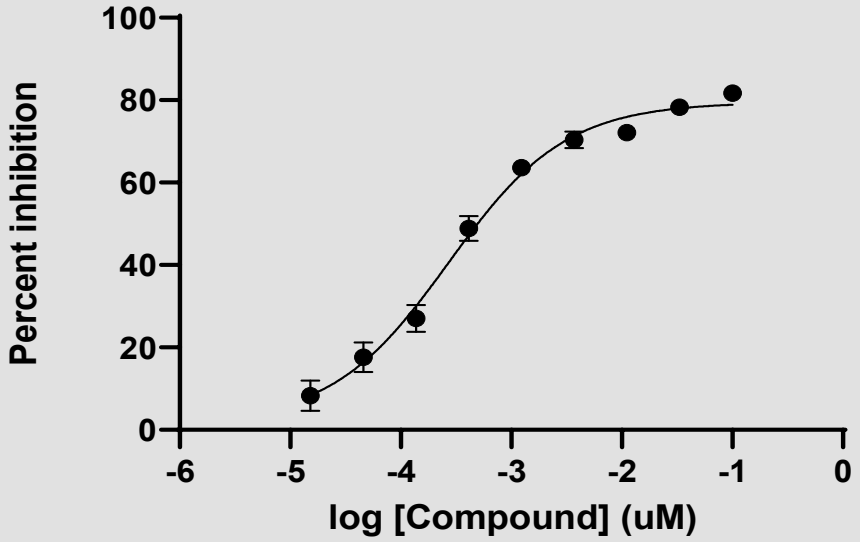


Adapted from Gonzalez-Gay et al, Autoimmunity Rev, (2020) 19: 102429 and Rusinol and Puig, Int J Mol Sci, (2023) 24: 3391

Demonstrated Potency Against Th17 Cytokines

VYN202 Potency vs. IL-17A compares favorably to Secukinumab and DC-806

VYN202 Potency vs. IL-17A



Therapeutic Agent	$IC50_{IL17A}$ (nM)
VYN202 (VYNE)	0.27
Secukinumab (Cosentyx - NVS):	0.37
DC-806 (DICE/LLY)	5.7

Cytokines were analysed by ELISA with media supernatant from cultured human PBMCs activated with anti-CD2, CD3 & CD28 antibodies in the presence or absence of compounds for 72h.

Source: Data on file; Summary basis of approval for Cosentyx, pharmacology review, CDER, FDA, August 2014; Dice Therapeutics Corporate Presentation March 2023

Minimal Inhibition on Key Innate Immune Chemokine Demonstrates Selectivity of Cytokine Expression (IL-17A and IL-22 vs. CXCL10)

Cytokine	VYN202 IC_{50} (nM)	Selectivity vs. CXCL10
IL-17A	0.27	>13,000
IL-22	0.21	>17,000
CXCL10	3637	-

- **VYN202 significantly more potent against Th17 Cytokines vs. CXCL10**
- CXCL10 interacts with CXCR3 to attract Th1 cells, eosinophils, monocytes, and NK cells to sites of inflammation and is known to be an important part of host defense mechanism

Analysed by ELISA with media supernatant from human PBMCs stimulated with IFN-γ for 24h.

Source: Data on file

VYNE™ THERAPEUTICS

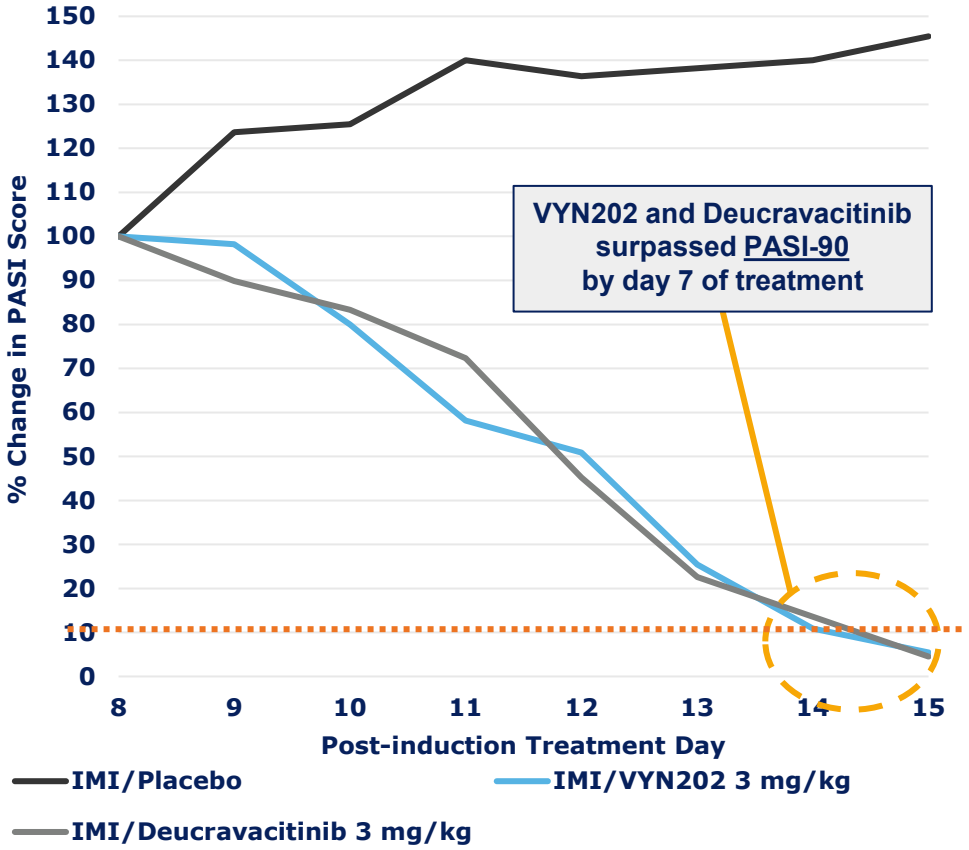
Preclinical Efficacy Models

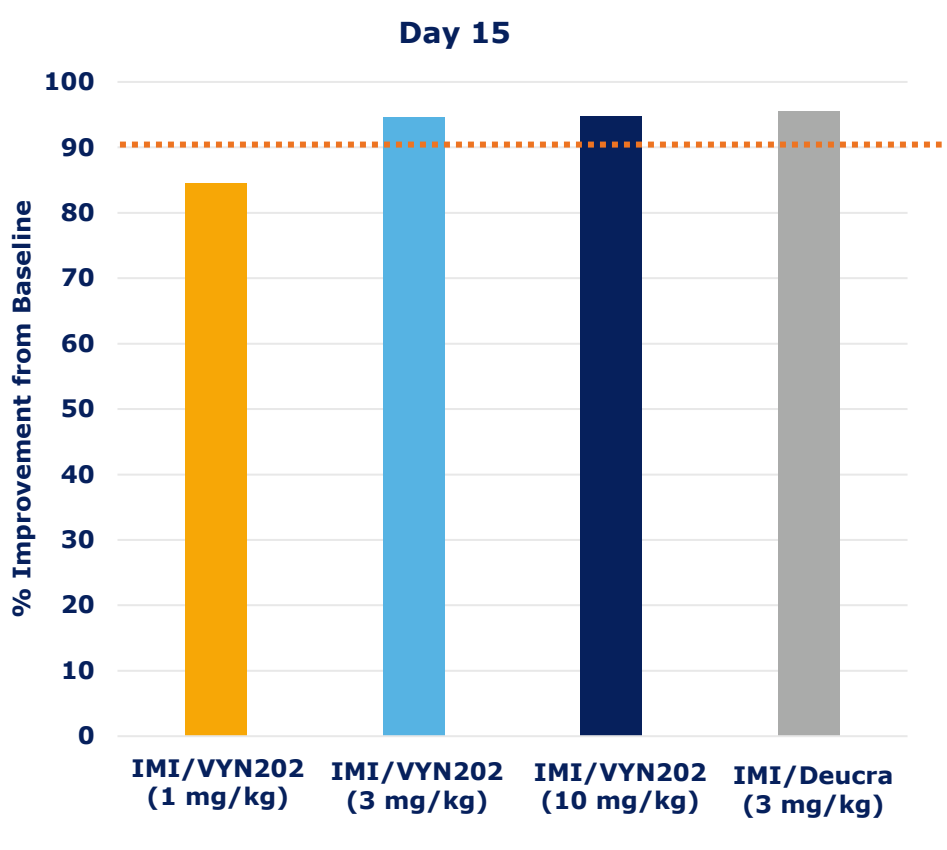
VYN202: Psoriasis Model

VYNE™ THERAPEUTICS

VYN202: Comparable Onset of Action and Efficacy to Deucravacitinib[1]
at Equivalent Dosing in Preclinical *in vivo* Model of Psoriasis

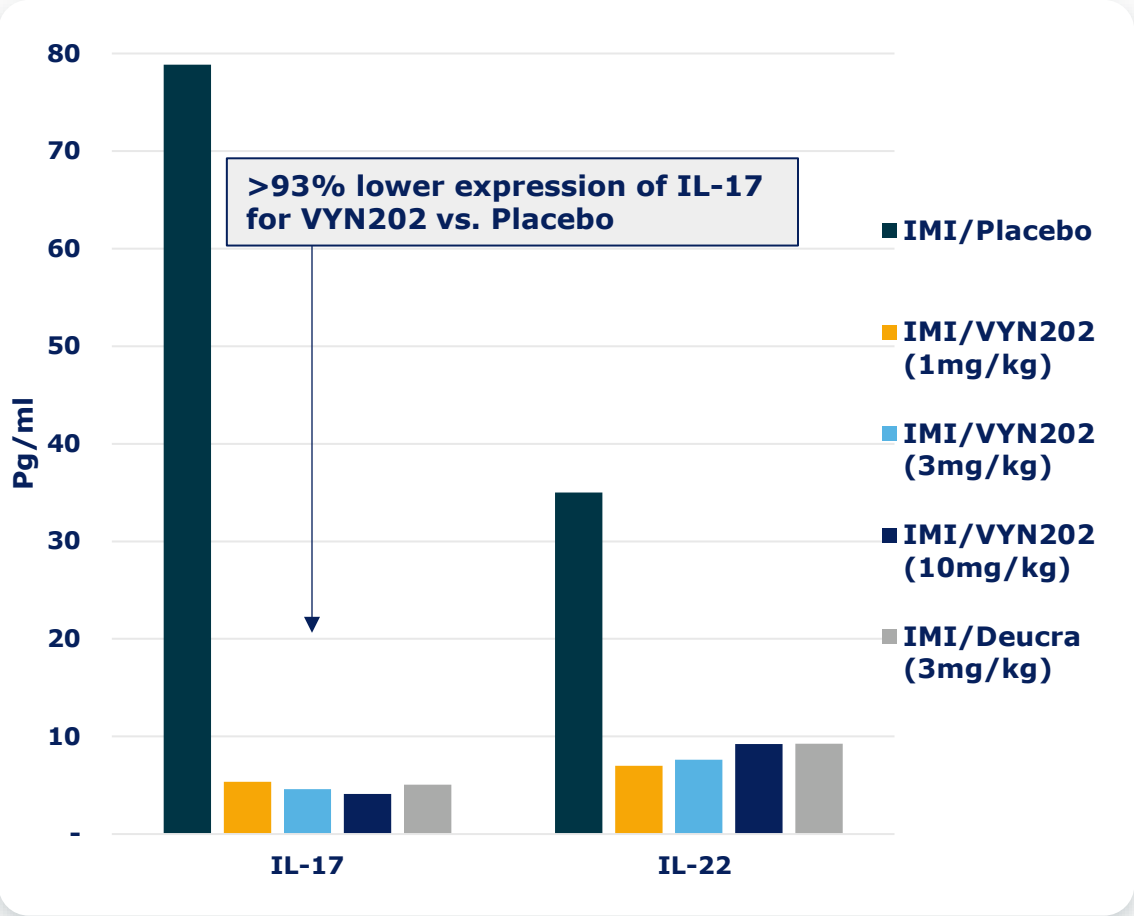
Dorsal depilated BALB-C mice were dosed for 14 days with topical imiquimod cream (Day 1-7: induction phase, Day 8-14: treatment phase). N=8 animals were assigned to each treatment group and received 3 mg/kg of allocated treatment intraperitoneally dosed once-daily on Day 8-14.

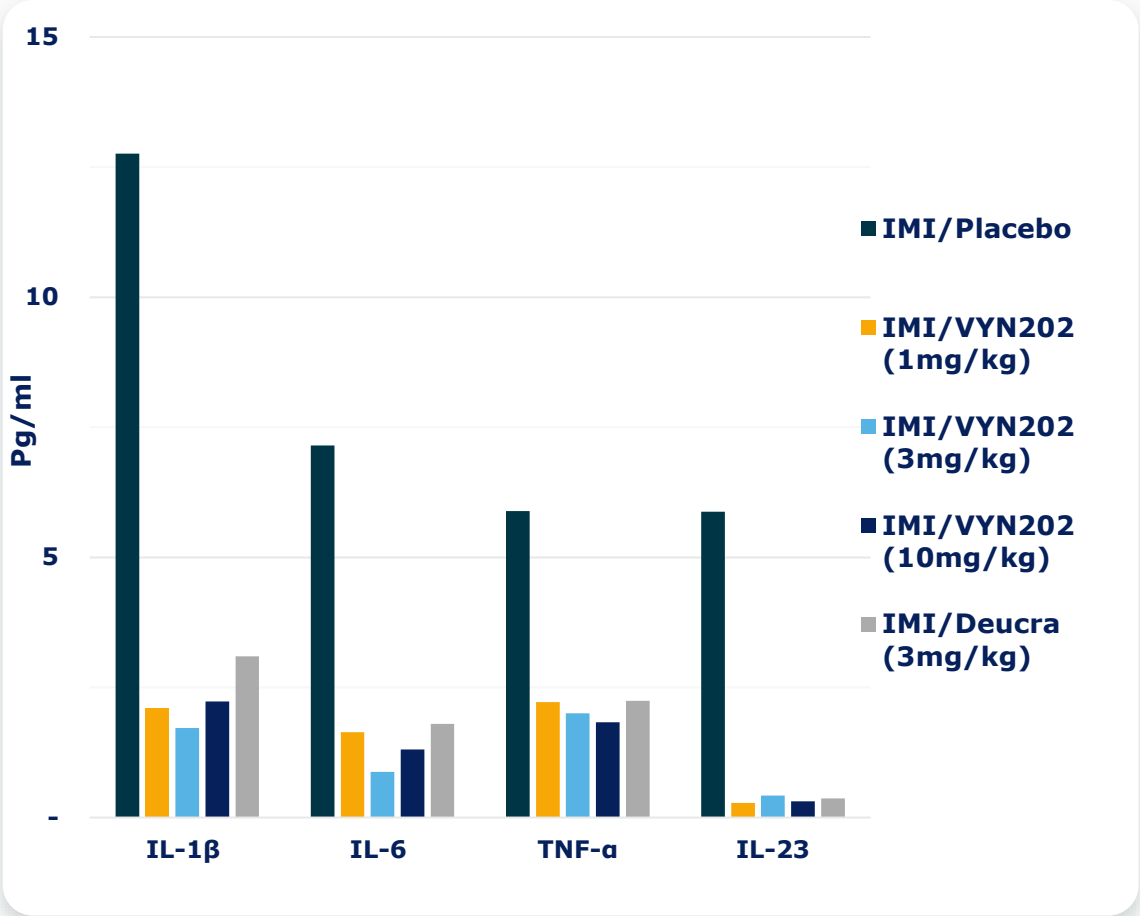




1Sotyktu® (deucravacitinib) was approved in the U.S. in September 2022.
PASI-90 = 90% improvement from baseline in PASI score

VYN202 Reduced Key Cytokines Associated with Pathogenesis of Psoriasis
in Preclinical *in vivo* Model





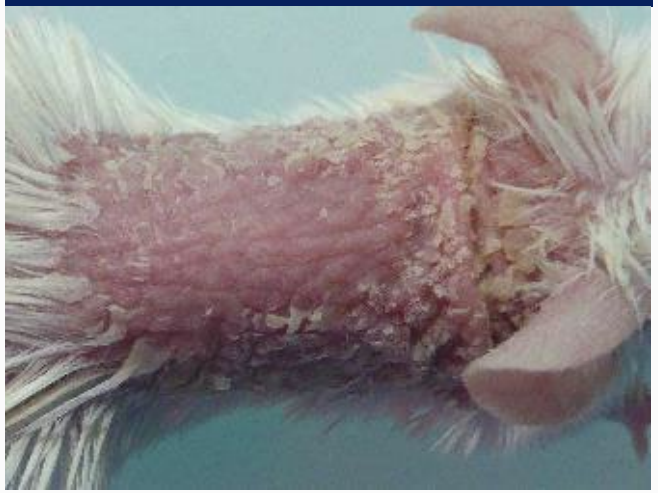
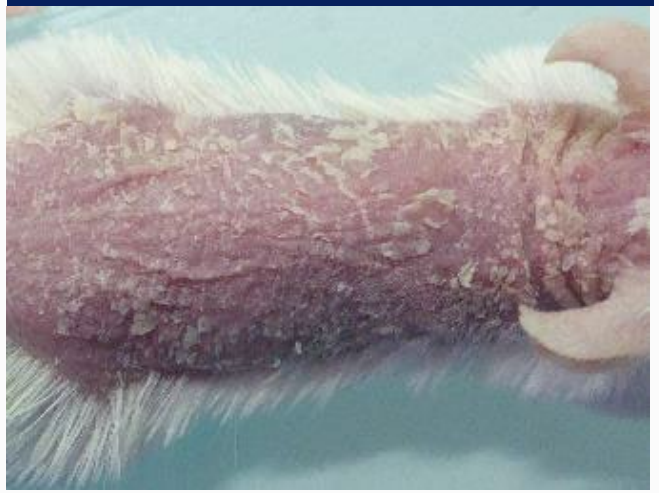
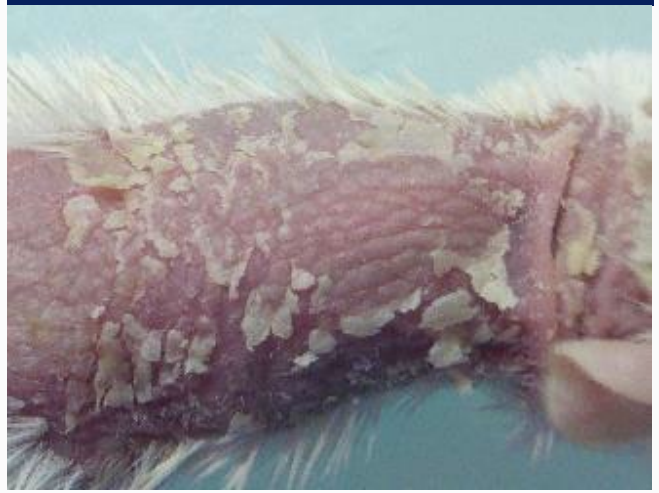
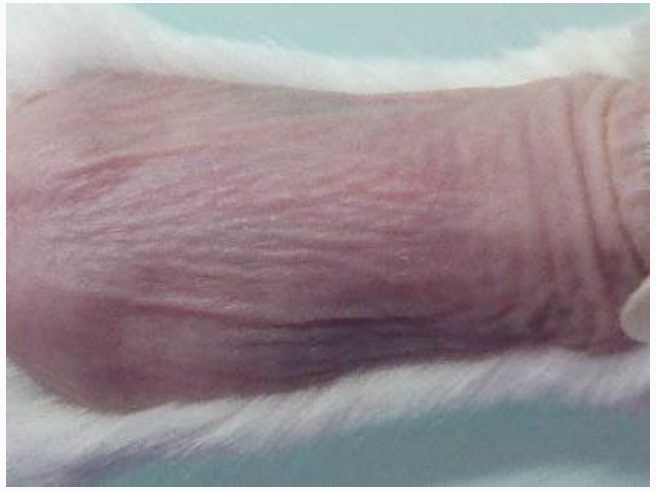
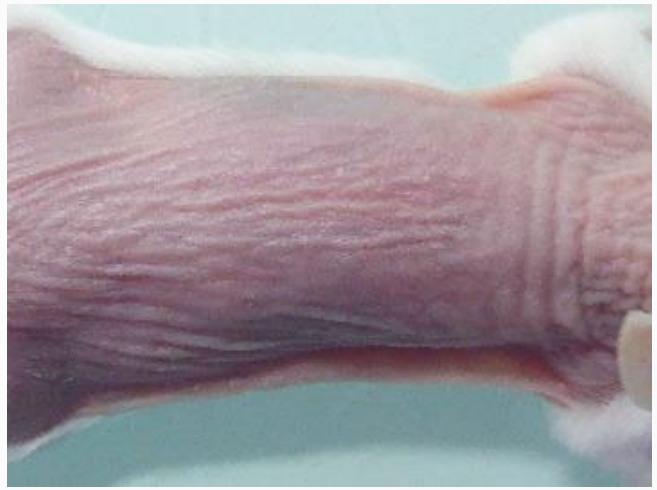
- >93% lower expression of IL-17 at all VYN202 doses compared to placebo

- Marked reduction of other disease related Th17 and Th1 cytokines

IMI = imiquimod

VYN202: Marked Improvement in Clinical Presentation of Disease

Comparable to deucravacitinib in resolving induced dermal inflammation at an identical dose after 7 days of treatment

	IMI/Placebo	IMI/VYN202 3mg/kg	IMI/Deucravacitinib 3mg/kg
Day 8 Before treatment			
Day 15 After 7 days of treatment			

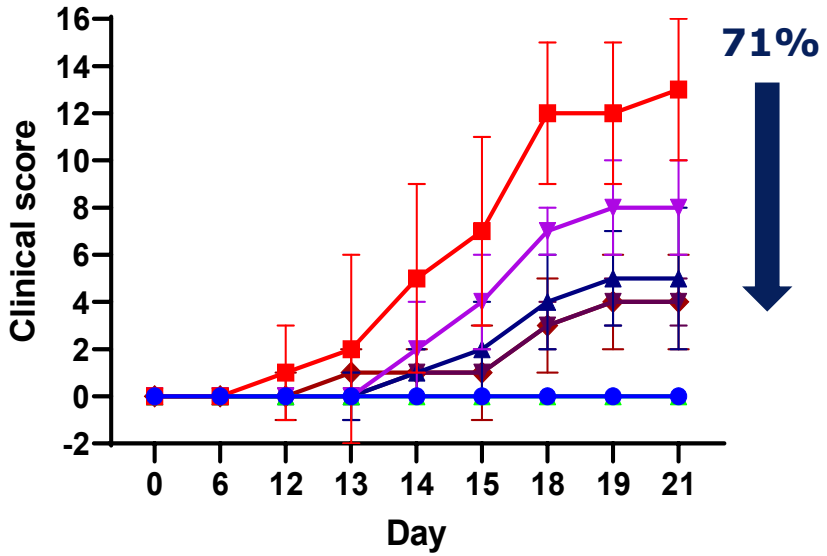
IMI = imiquimod;

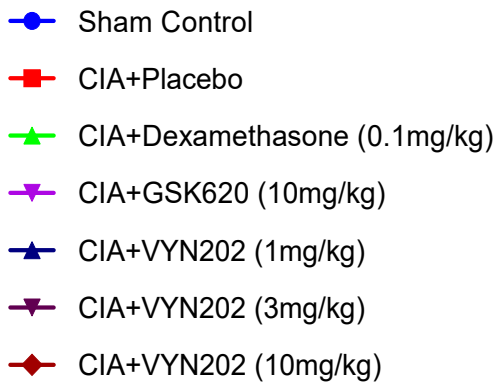
VYN202: Rheumatoid Arthritis Model

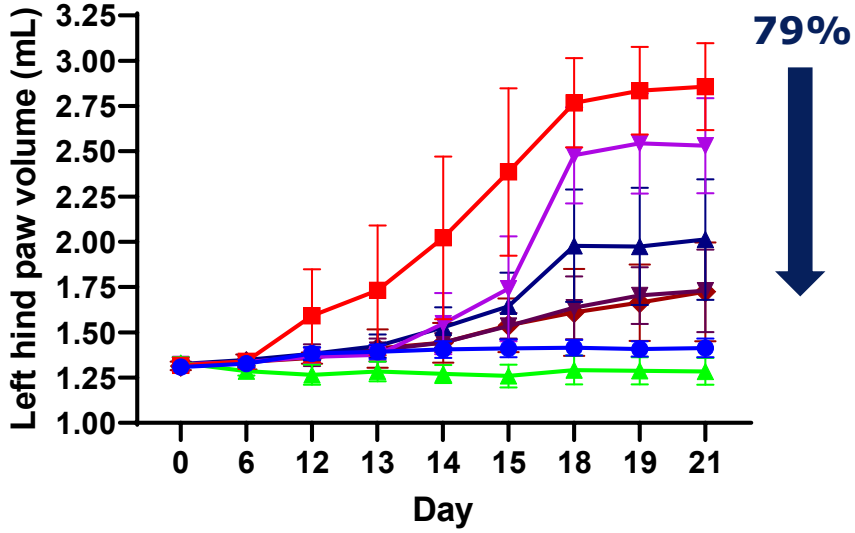
VYNE™ THERAPEUTICS

VYN202: Collagen-Induced Arthritis Model in the Rat – Arthritis Score

- VYN202 demonstrated highly potent anti-inflammatory activity
- VYN202 statistically superior to GSK620 (BD2-selective BET inhibitor) at all dose levels







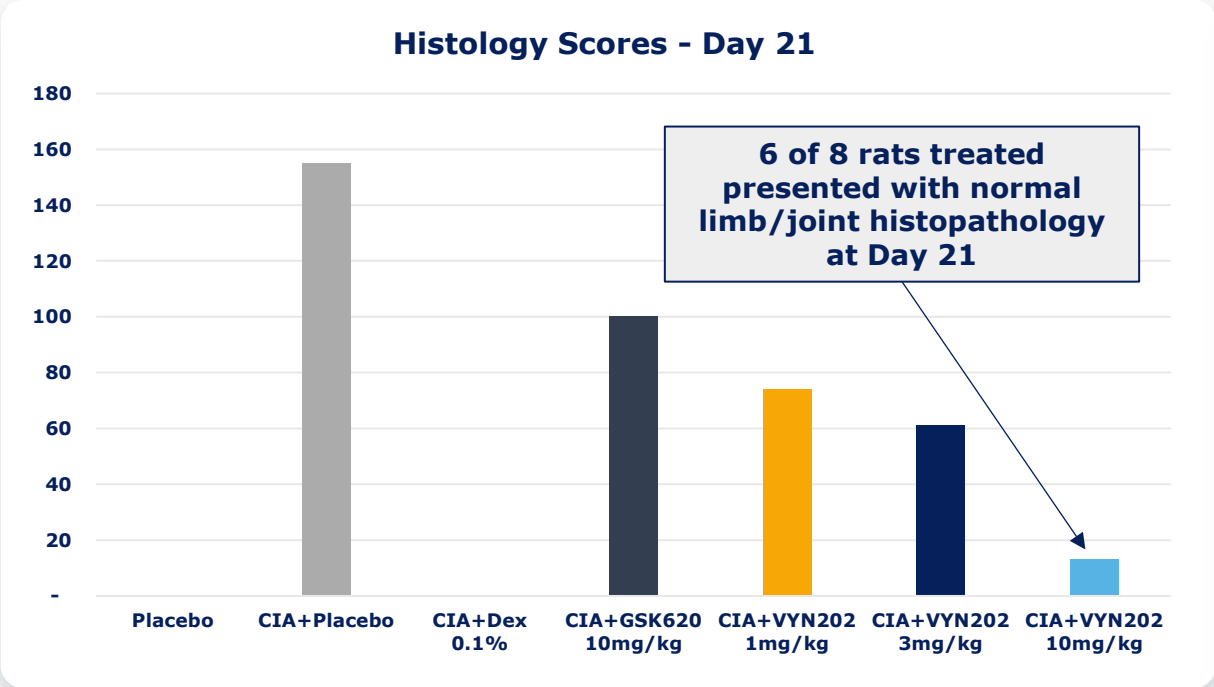
- VYN202 10mg/kg PO QD treatment resulted in a 71% lower clinical score and 79% lower paw volume compared to CIA+Placebo control at Day 21
- All VYN202 treatment groups were statistically significantly superior to both CIA+Placebo and GSK620 10mg/kg PO QD controls

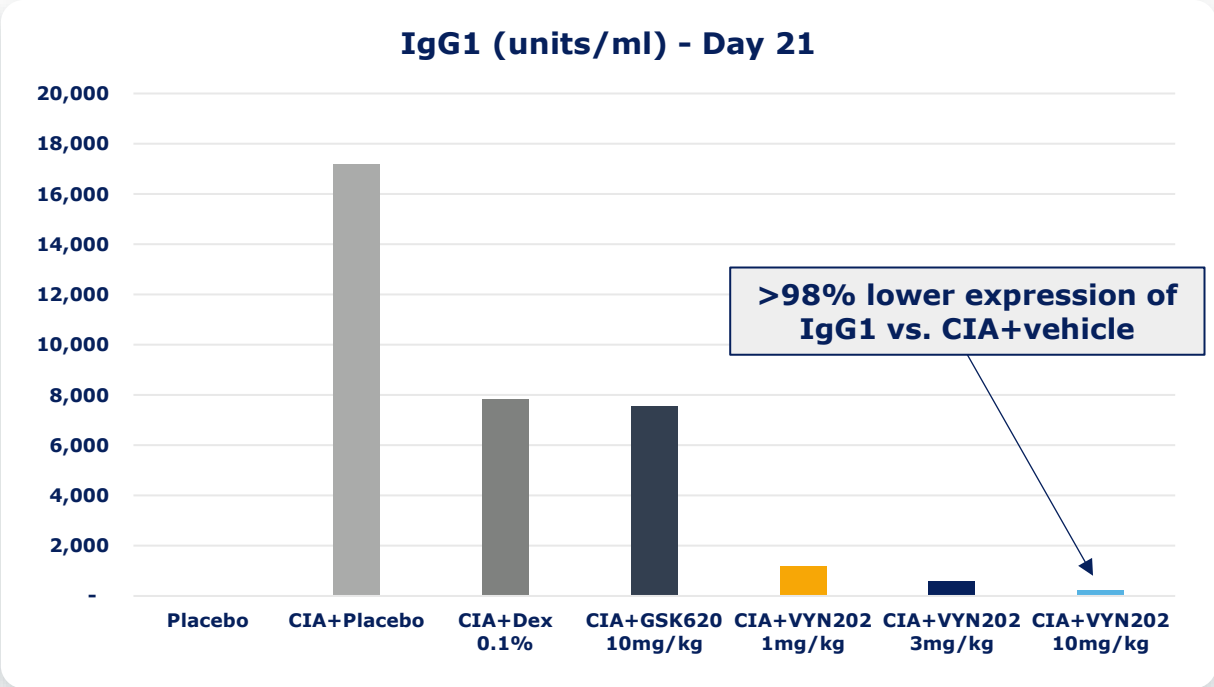
Inflammatory arthritis was induced in Lewis rats using a mixture of collagen and CFA by IV injection at Day 0 and was further challenged with a collagen and IFA IV injection at Day 7 (N=8/treatment group). Treatment groups received oral doses QD for 21 days. Clinical score was evaluated for all four limbs with scoring range from 0 (normal) to 4 (extensive signs and symptoms of arthritis); Maximum clinical score: 16

VYNE™ THERAPEUTICS

VYN202: Collagen-Induced Arthritis Rat Model – Histology Score & Biomarkers

- Treatment with VYN202 at 10mg/kg PO QD results in near normal joint histopathology
- VYN202 demonstrated near complete inhibition of IgG1* expression at all doses





- CIA+VYN202 treatment resulted in a dose-dependent reduction in severity of arthritic histopathology & was statistically superior to CIA+Placebo and CIA+GSK620 at all doses
- VYN202 10mg/kg PO QD reduced the expression of IgG1 by >98% vs. CIA+Placebo control & was statistically equivalent to Placebo control

*Immunoglobin G1

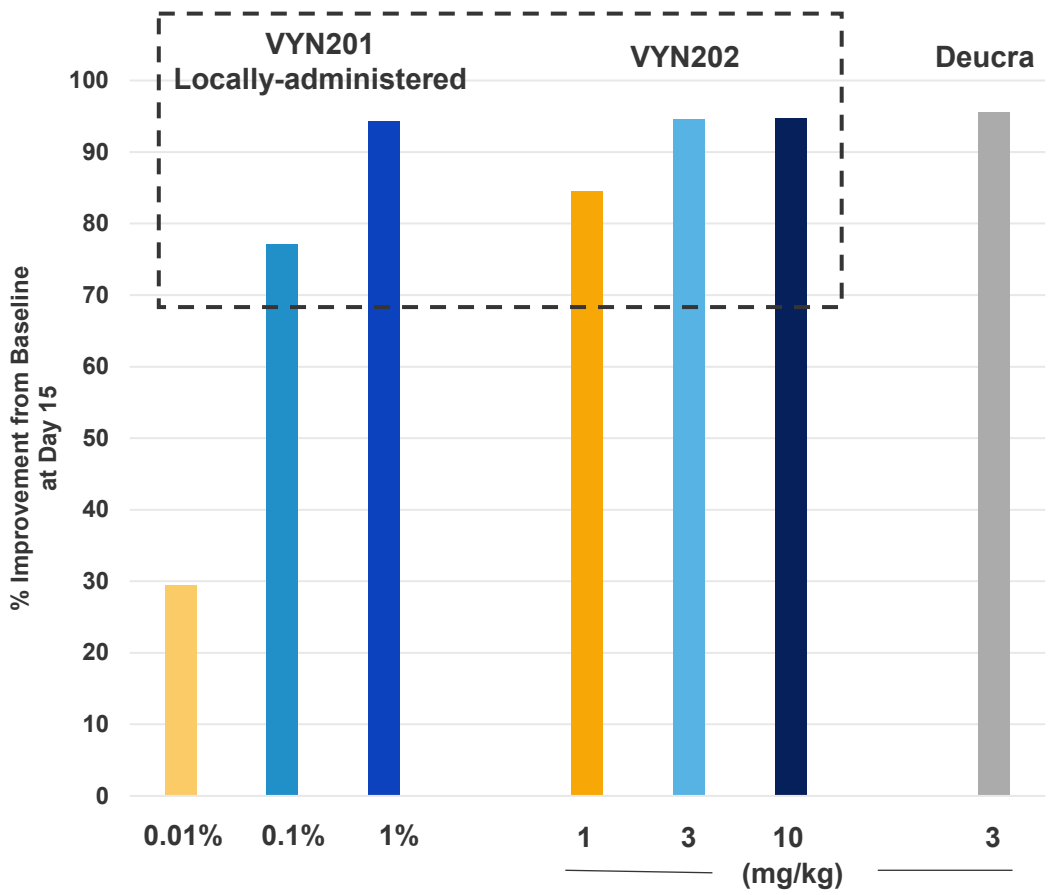
Note: Histology - Mixed cell inflammation; tissue granulation; increased bone, periosteum; increased eroded surface bone and cartilaginous erosion/ulceration were assessed on a 4-point severity scale: minimal (1), mild (2), moderate (3) and marked(4). Composite histopathology score was calculated by summing each assessment by severity and incidence. Maximum score: 160 (5 x 4 x N=8/group).

VYNE™ THERAPEUTICS

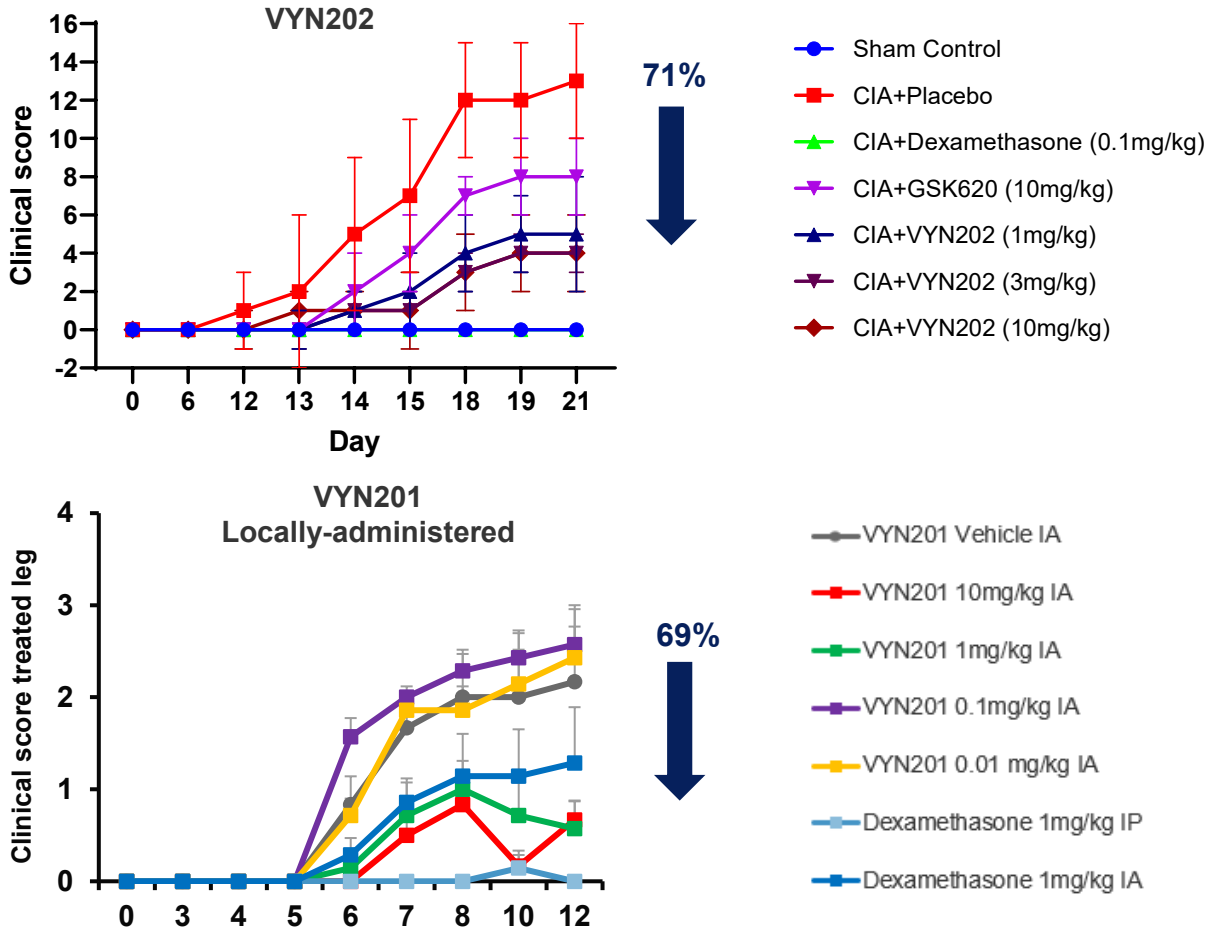
VYN202 Results Show Strong Correlation with VYN201 Results

Reinforcing BET potential and role of BD2 inhibition in treatment of autoimmune diseases

Psoriasis Model



Arthritis Model



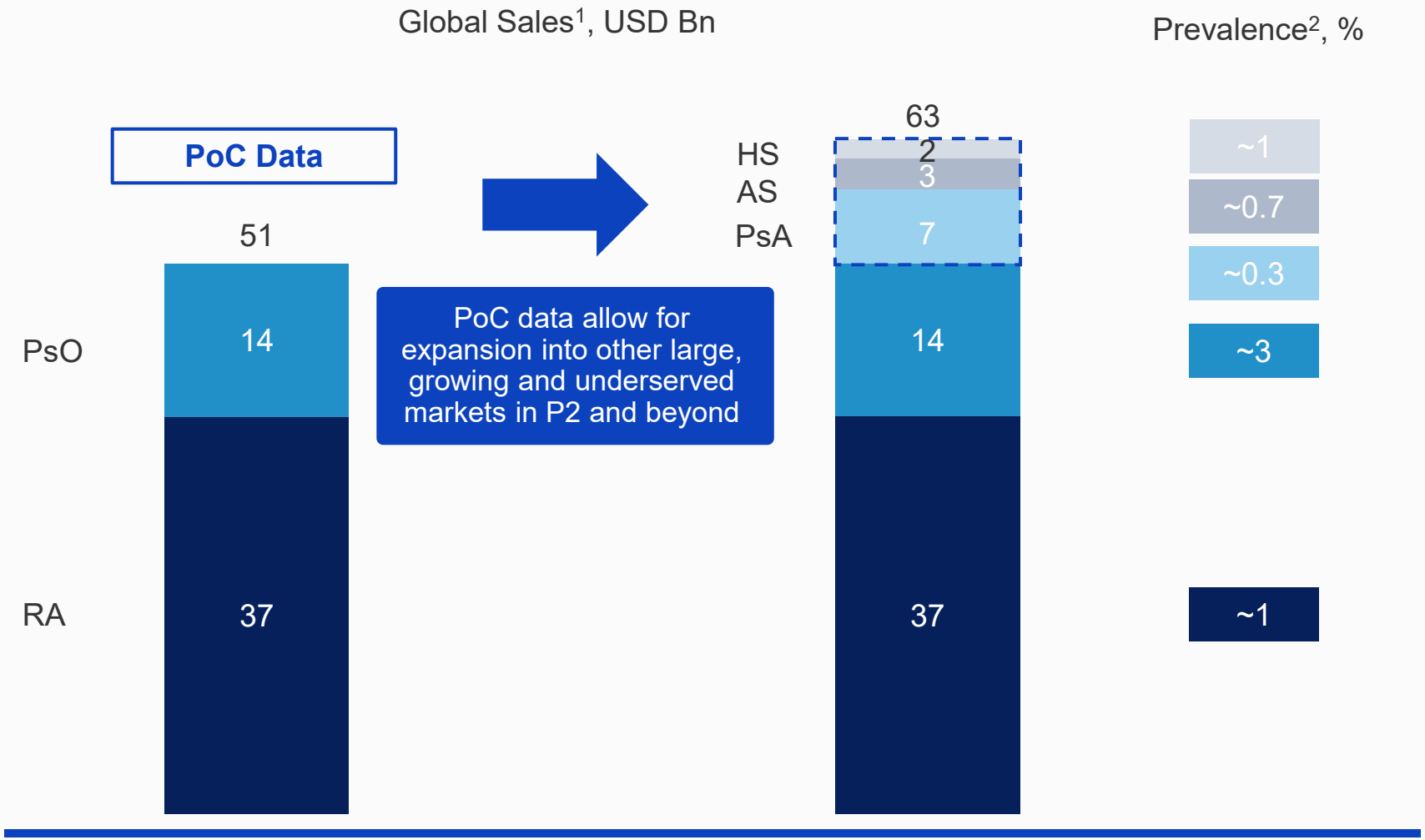
VYN202 Clinical Development Plan

1. Moderate-to-Severe Psoriasis
2. Moderate-to-Severe Active Rheumatoid Arthritis

VYNE™ THERAPEUTICS

Clinical Development Strategy

Initial PoC studies in psoriasis and rheumatoid arthritis serve as potential gateway to other large, strategically attractive markets



VYN202's impact on multiple inflammatory pathways unlocks potential for broad development strategy across range of immune-mediated diseases

Based on MOA and preclinical data, additional opportunities in other disease areas across:

- Dermatology
- Rheumatology
- GI
- Pulmonology and
- Oncology

Source: 1. Global Data; ABBV 2020 Long-term Strategy Corporate Presentation; Data on file 2. Alotaibi HM Clin Cosmet Investig Dermatol. 2023; MacGearailt C., Fitzgerald, G. EMJ Rheumatol. 2021; Ogdie A, Weiss P. Rheum Dis Clin North Am. 2015; Armstrong, et al. JAMA Dermatol. 2021; RA Xu Y, Wu Q. J Clin Med. 2021

VYN202 Preliminary Study Designs

Healthy Volunteers

SAD

Placebo-controlled study evaluating safety, tolerability, PK and PD

- Trial size: N=~40
  Evaluated 5 cohorts of VYN202 (N=8 / cohort) including food effect

Complete

MAD

- Trial size: N=~24
  Evaluating 3 strengths of VYN202 once-daily for 14 days (N=8 / cohort)
- Strengths evaluated to be determined by SAD results
- Measurement of key biomarkers

Results anticipated in Q4 2024

PoC Studies in Patients with Disease

Psoriasis (Mod/Severe)

- Multicenter, double-blind, placebo-controlled phase 1b study
- Trial size: N=~40
  3:1 randomization to treatment with oral VYN202 capsules (low dose, high dose) or placebo once daily in two ascending cohorts
- Duration: 12 weeks
- Entry criteria: Subjects aged 18+ with a clinical diagnosis of moderate-to-severe plaque psoriasis (IGA≥3, PASI≥12).
- Safety/tolerability, PK, PD biomarkers, exploratory efficacy (%CFB PASI, Proportion of subjects ≥PASI50, 75 and 90)

Rheumatoid Arthritis (Mod/Severe)

- Multicenter, double-blind, placebo-controlled phase 1b study
- Trial size: N=~40
  3:1 randomization to treatment with oral VYN202 capsules + MTX (low dose, high dose) or placebo + MTX once daily in two ascending cohorts
- Duration: 12 weeks
- Entry criteria: Subjects aged 18+ with a clinical diagnosis of adult-onset moderate-to-severe active rheumatoid arthritis (≥4 target joints, DAS28-CRP ≥3, hsCRP≥5µg/ml) on a stable dose of MTX for 90 days.
- Safety/tolerability, PK, PD biomarkers, exploratory efficacy (DAS28-CRP and ACR20/50/70 and %CFB in hsCRP.

PoC studies expected to be initiated following successful SAD/MAD results with TLR anticipated in 2H 2025

PoC data in PsO and RA provide significant optionality and unlock potential opportunities in other indications such as PsA, AS and HS in P2 and beyond

Current estimates, subject to change

VYN202 Program Summary

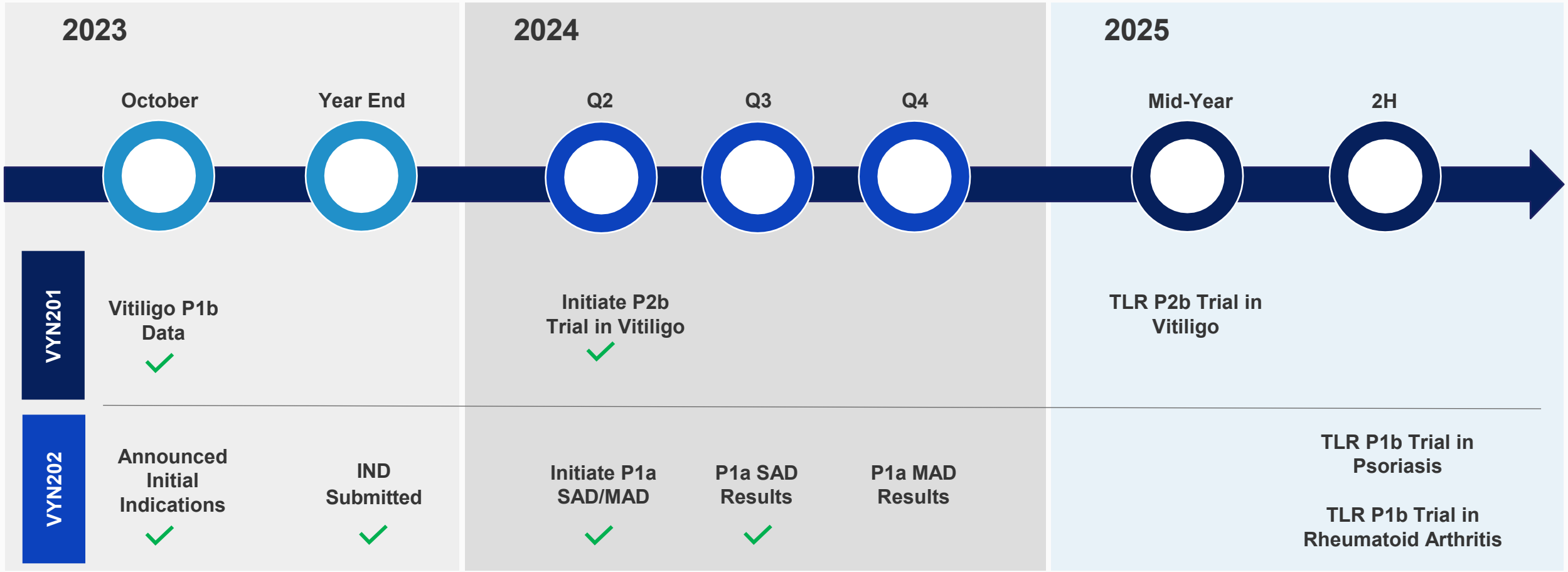
- Novel, highly differentiated MOA - acting at the point of gene transcription in T Cells to directly address the complex signaling of immuno- & fibro-inflammatory diseases
- BET Inhibition's impact on multiple inflammatory pathways unlocks potential across broad range of immune-mediated diseases

- Historical pan-BD BET safety concerns addressed via potential class-leading selectivity and potency vs. BD2 binding domain

- Strong preclinical data across multiple diverse models of autoimmune disease demonstrating significant down regulation of key pro-inflammatory & disease-related biomarkers with corresponding improvements in disease severity

- VYN202 preclinical efficacy results show strong correlation with VYN201 results reinforcing drug design thesis and BET inhibition potential in psoriasis, rheumatoid arthritis, and other TH17 driven diseases

Multiple Paths to Potential Value Creation Across BET Inhibitor Programs



Based on current estimates.

NASDAQ: VYNE

Appendix

VYNE™ THERAPEUTICS

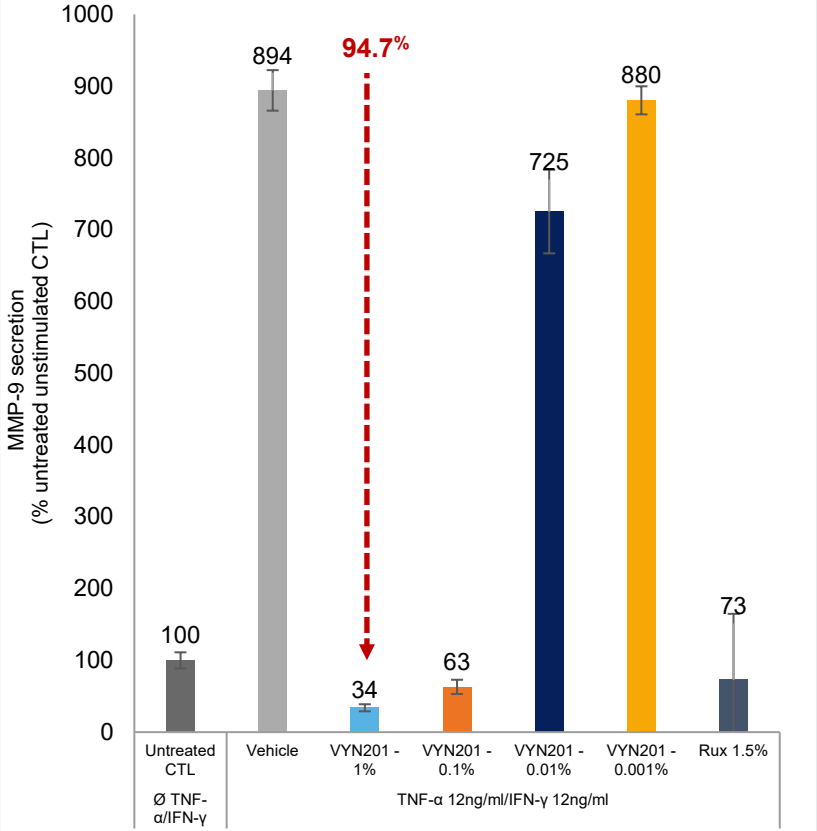
VYN201: Preclinical Data

VYNE™ THERAPEUTICS

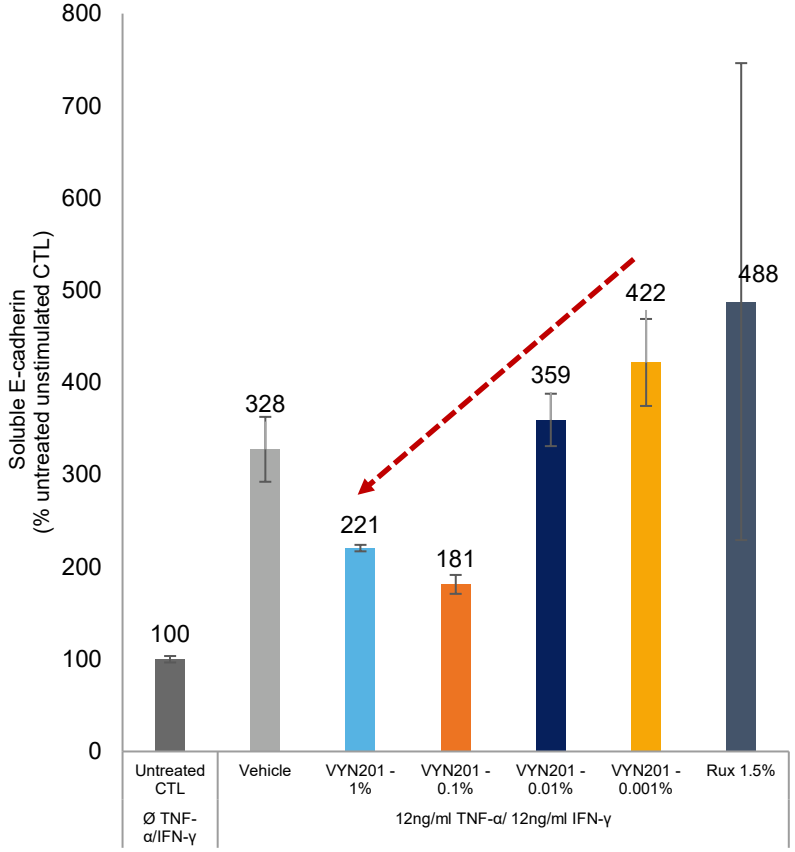
VYN201: Human Tissue Model of Vitiligo

Demonstrated reduction in melanocyte loss and lowering of key inflammatory biomarkers

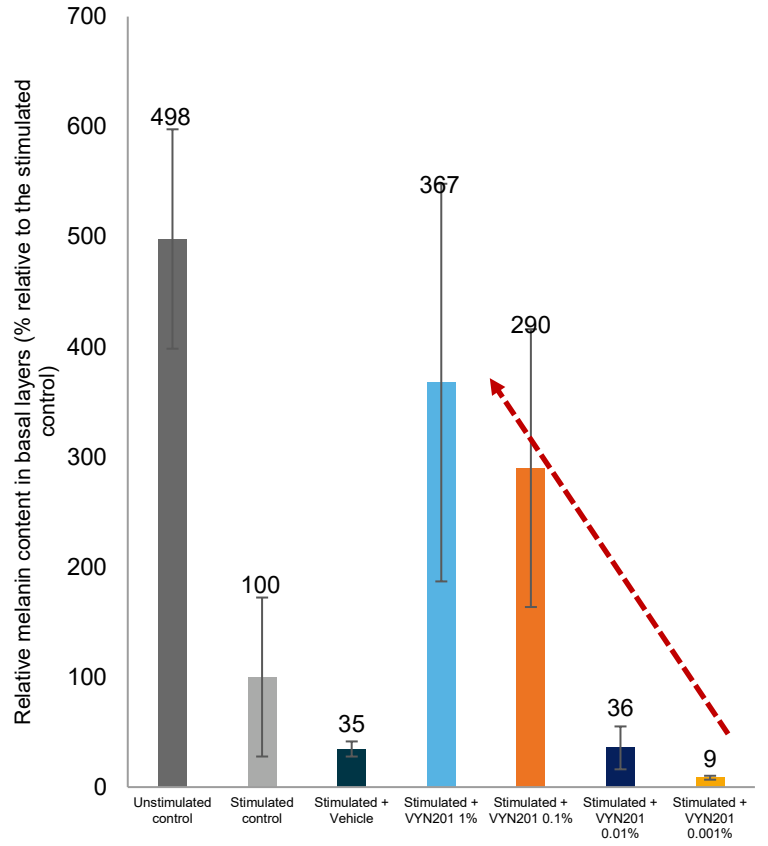
VYN201 1% **reduced the secretion of MMP9** relative to stimulated vehicle, and numerically superior to ruxolitinib 1.5%



VYN201 affects a **dose-dependent reduction in solubilized E-cadherin**



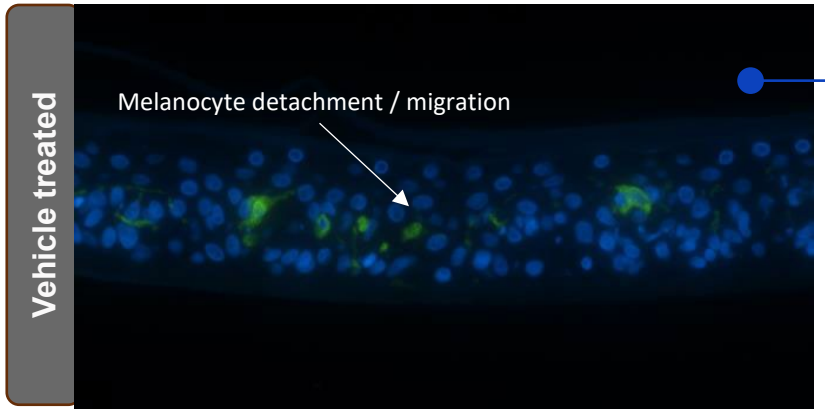
VYN201 **substantially prevents the loss of melanin** pigment in the basal layers of skin in a dose dependent manner



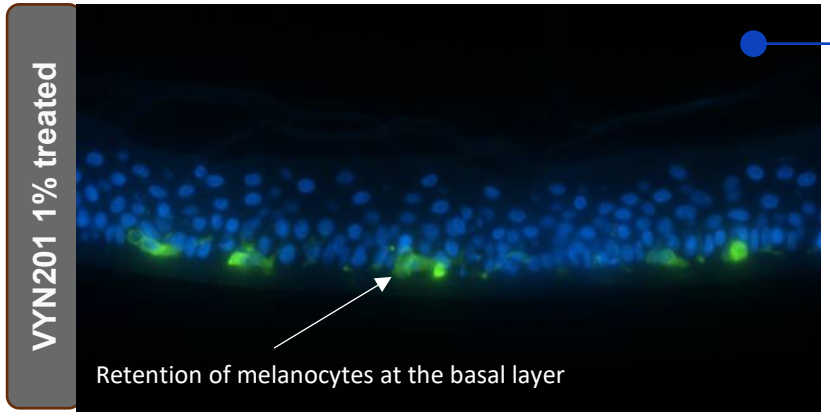
Reconstituted human epithelial (RHE) skin cultures were treated with a TNF-α and IFN-ɣ cytokine cocktail to induce a vitiligo phenotype melanocytorrhagy (loss of melanocyte), upregulation of MMP9 and soluble E-cadherin).

VYN201: Human Tissue Model of Vitiligo

VYN201 prevents melanocyte detachment, down regulates the expression of key cytokines and upregulates WNT pathway



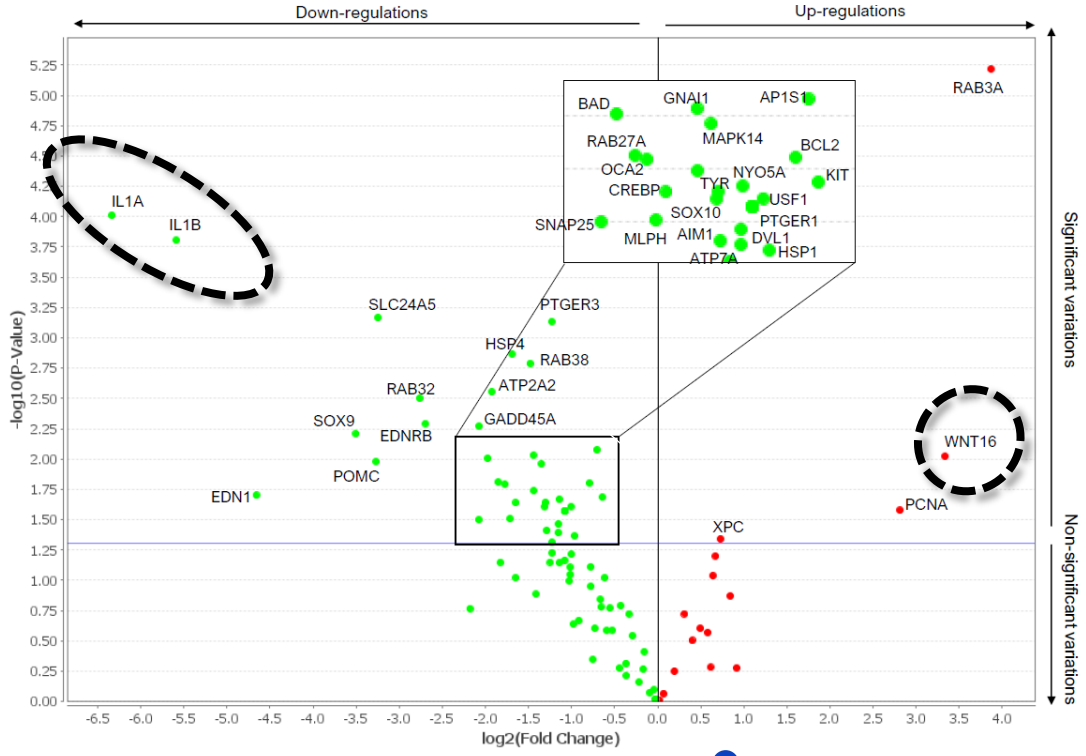
Clear evidence of melanocyte adhesion disruption, melanocyte detachment and migration through the skin



VYN201 1% prevents detachment and subsequent loss of melanocytes from the basal layer implying that E-cadherin adhesion is still functional

Keratinocytes (blue), melanocytes (green)

Stimulated and VYN201 1% treated



Significant downregulation of cytokines IL6, IL1A and IL1B and TNFa and upregulation of the WNT pathway (Wnt16)

TRV: tyrosinase-related protein 1 (important enabler of melanogenesis)

VYN201: Phase 1 Proof-of-Concept

VYNE™ THERAPEUTICS

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

Adverse Events

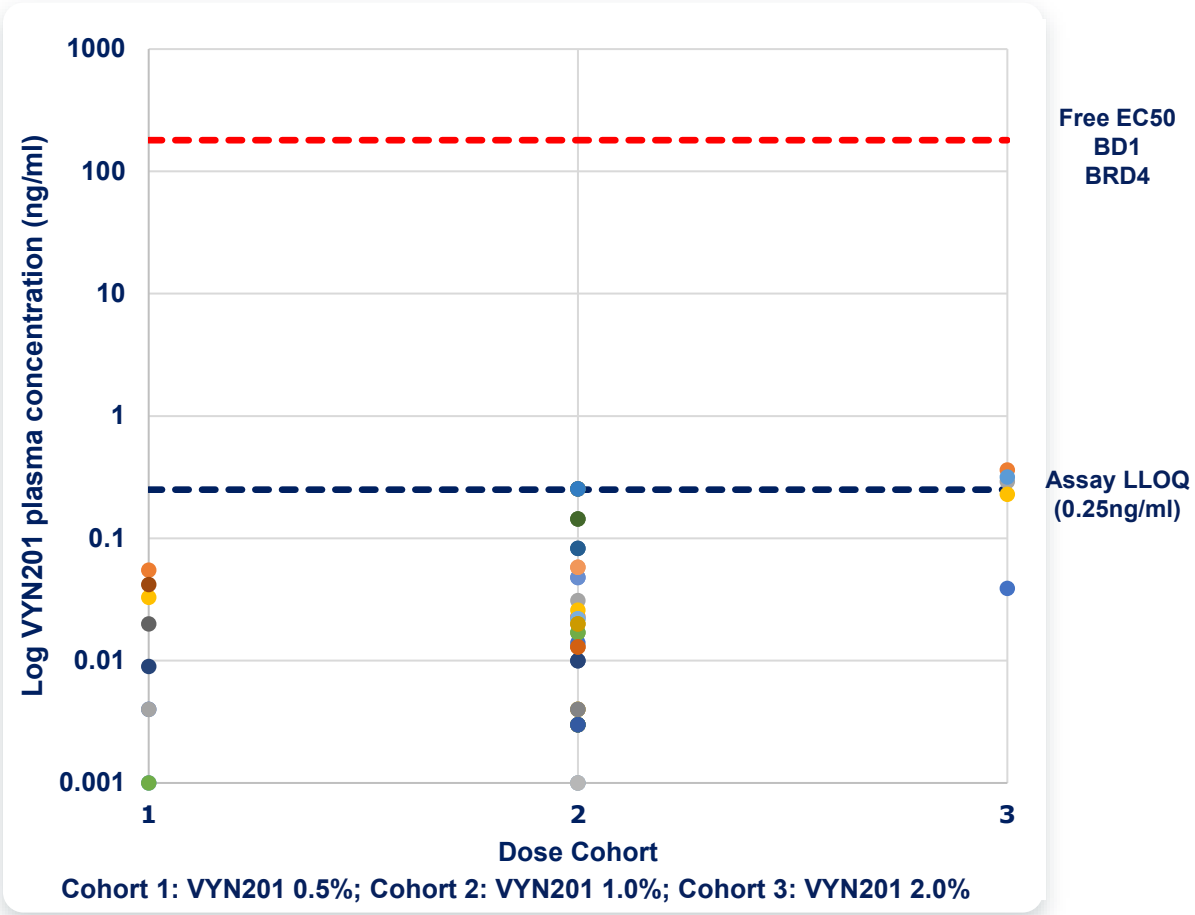
- **No** serious adverse events reported
- **No** treatment related discontinuations
- **All** TEAEs classified as **mild (>70%) or moderate**; except for 2 severe events of application site pain reported for 1 subject in 2% cohort which resolved
- **No** dose/exposure-dependent increases in AEs
- **No**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

Local Skin Tolerability

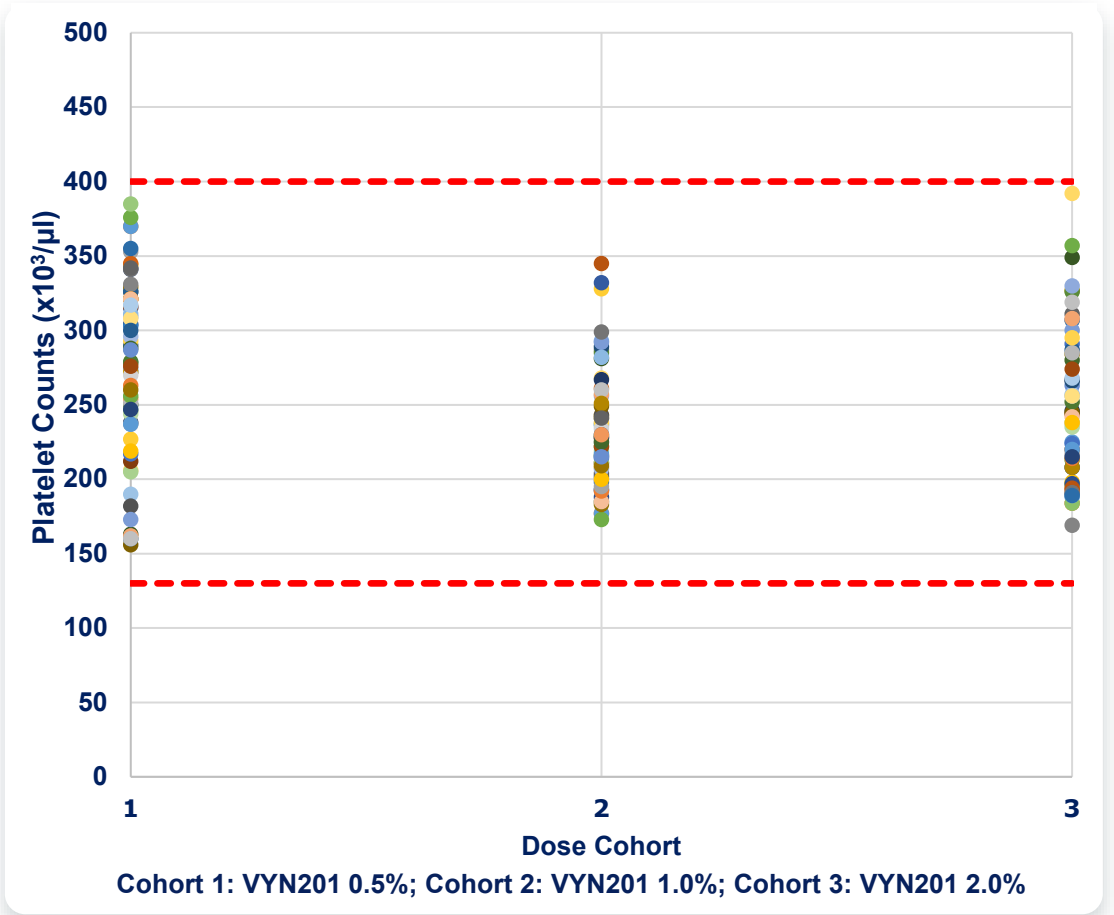
Assessment	Mean Score Range 0 (None) to 3 (Severe)
Burning/Stinging	0.26
Scaling	0.15
Dryness	0.22
Pruritus	0.14
Erythema	0.29
Hyperpigmentation	0.10

VYN201 Phase 1b: Low Systemic Exposure in Vitiligo Subjects Correlates with No Impact on Platelet Counts

Available data for treatment up to 16 weeks supports "soft" drug approach for topical pan-BD BET inhibitor



Cohort 1: VYN201 0.5%; Cohort 2: VYN201 1.0%; Cohort 3: VYN201 2.0%



Cohort 1: VYN201 0.5%; Cohort 2: VYN201 1.0%; Cohort 3: VYN201 2.0%

- VYN201 concentrations markedly below free EC50BD1 BRD4 at all dose levels for available data for treatment up to 16 weeks
- Assay LLOQ is 720-fold lower than the free $EC50_{BD1\ BRD4}$ for VYN201

- All platelet counts remain within normal range
- No trends suggestive of reducing counts by treatment duration
- Similar lack of effect on neutrophils, eosinophils, lymphocytes, basophils and monocytes (data not shown)

Data available as of 11/8/23 LLOQ = Lower Limit of Quantification