

Corporate PresentationMay 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



- 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



- 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 expected to be initiated in Q2 2024



- VYN201: Phase 2b trial expected to be initiated in Q2 2024, with top-line results anticipated in mid-2025
- VYN202: Phase 1a SAD/MAD read-out anticipated 2H 2024
 - (2) Phase 1b PoC studies in plaque psoriasis and rheumatoid arthritis planned, with top-line results anticipated in 2H 2025



- · Seasoned leadership team with demonstrated track record of progressing programs through regulatory approval
- Cash: \$86.0M¹; No debt
 Q4 2023 financing with syndicate of leading healthcare investors expected to provides cash runway through the end of 2025

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

Drogram	Indication(a)	Route of	Current Stage			Status / Next	Diahta	
Program Indication(s)	Administration	Preclinical	IND-Enabling	Phase 1	Phase 2	Anticipated Milestones	Rights	
InhiBET™ Platfo	InhiBET™ Platform - Library of NCE BET Inhibitors for Any Indication Worldwide							
VYN201 Soft pan-BD BET inhibitor	Nonsegmental Vitiligo	Topical					Phase 1 completedQ2 2024: Initiate P2bMid-2025: TLR P2b	Worldwide
VYN202 BD2-selective BET inhibitor	Moderate-to-Severe Plaque Psoriasis	- Oral					Q2 2024: Initiate P1a SAD/MAD 2H 2024: TLR P1a SAD/MAD	Worldwide
	Moderate-to-Severe Rheumatoid Arthritis							

Ongoing evaluation for other autoimmune and fibro-inflammatory diseases



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

BD₂

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

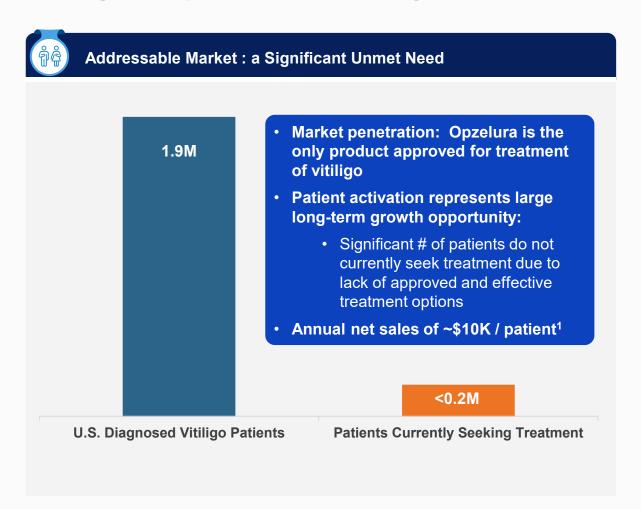


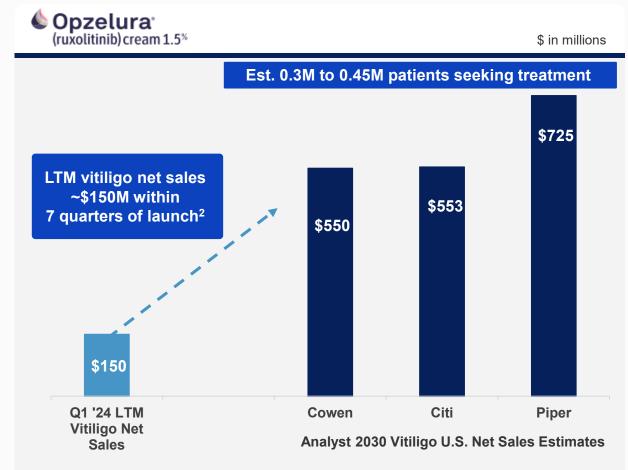


VYN201: Vitiligo



Vitiligo Represents a Large and Growing Market Opportunity





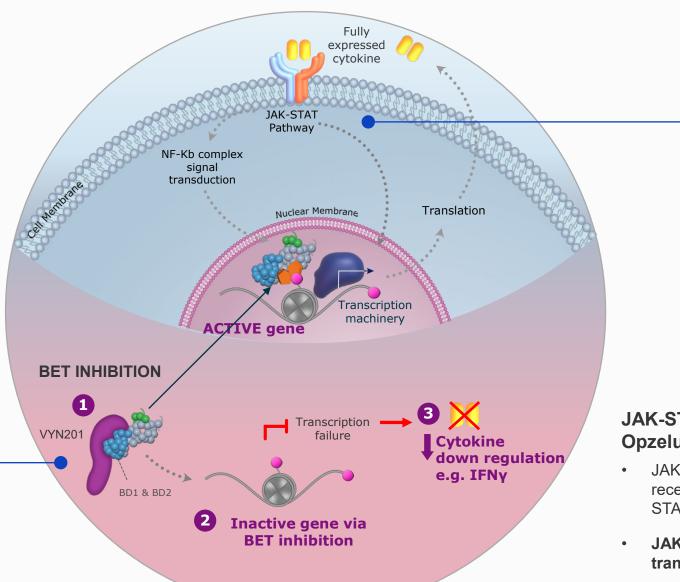
Only one drug approved, treatment is dominated by non-specific therapies including topical steroids and phototherapy

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

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.



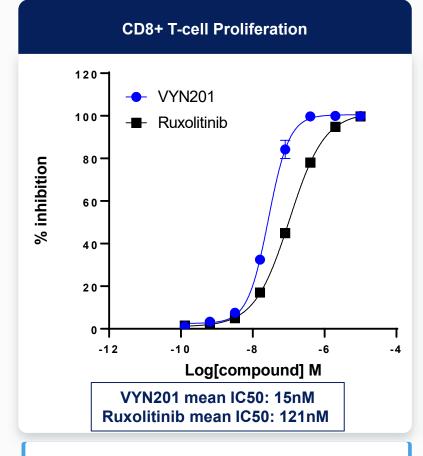
JAK-STAT pathway Opzelura® (ruxolitinib)

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

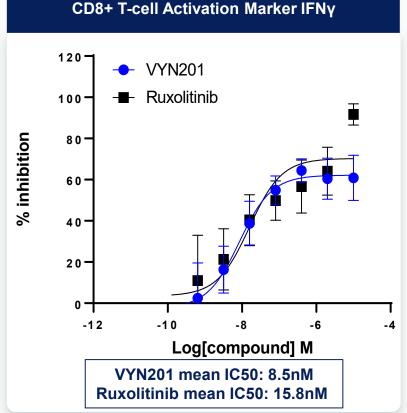
Adapted from Gonzalez-Gay et al, Autoimmunity Rev, (2020) 19: 102429 and Rusinol and Puig, Int J Mol Sci, (2023) 24: 3391

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

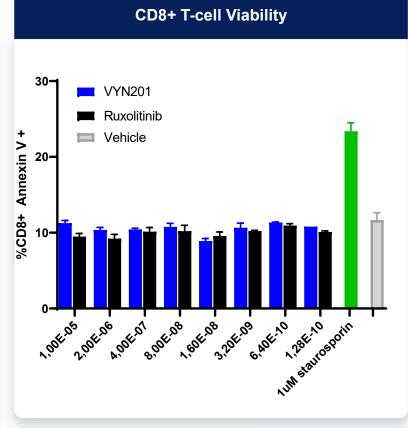
VYN201 has demonstrated marked inhibition of CD8+ t-cell expansion and activity at levels favorable to ruxolitinib



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







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

VYN201: Phase 1 Proof-of-Concept



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

Vitiligo Disease Activity within PoC Study Designs



Patient Population and Asset Development Status

	Disease Activity	Status
VYN201 P1b (VYNE)	Active Only	PoC achievedPhase 1b completed
Litfulo® (ritlecitinib) P2b¹ JAK3/TEC kinase inhibitor (Pfizer)	Active Only	 Pfizer currently enrolling P3 studies evaluating 50 mg QD dose in active & stable disease
Opzelura® (ruxolitinib) P2b³ JAK1/JAK2 inhibitor (Incyte)	Active & Stable	 1.5% BID dose approved in the U.S. (July 2022) and EU (April 2023)
Povorcitinib P2b ² JAK1 inhibitor (Incyte)	Active & Stable	Incyte currently enrolling P3 studies
Rinvoq [®] (upadacitinib) P2b ⁴ JAK1/JAK2 inhibitor (AbbVie)	Active & Stable	Phase 2b completed

VYNE expects to enroll 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 Therapy⁵

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



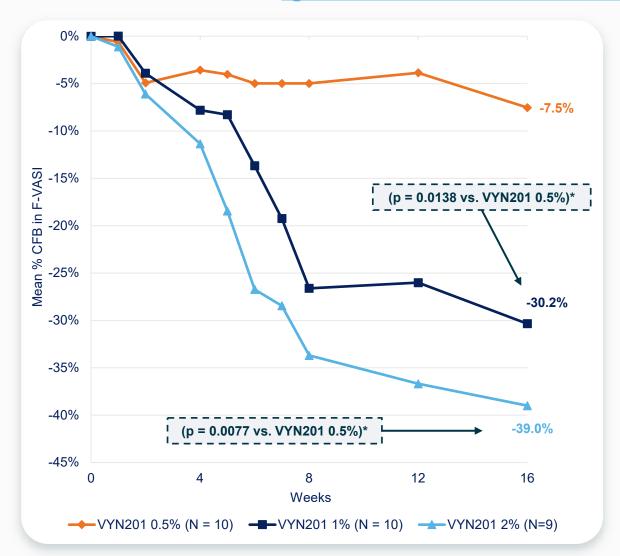
Fig 2:
16 weeks later
Showing extension
of depigmentation
and new areas of
confetti-like
depigmentation

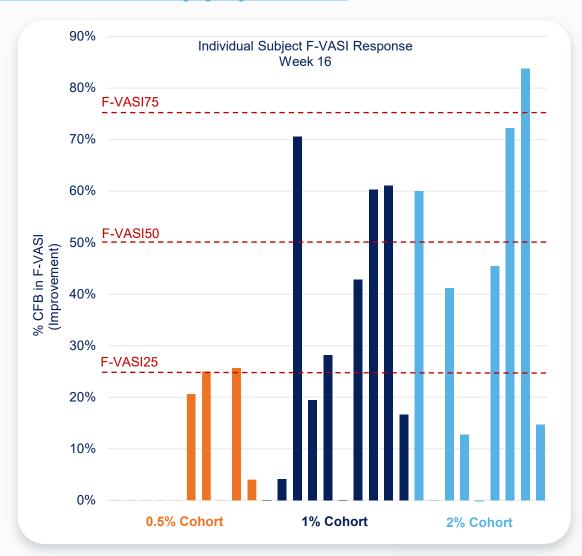


Physicians expect patients with active disease to be more difficult to treat

Promising Onset of Action and F-VASI Response

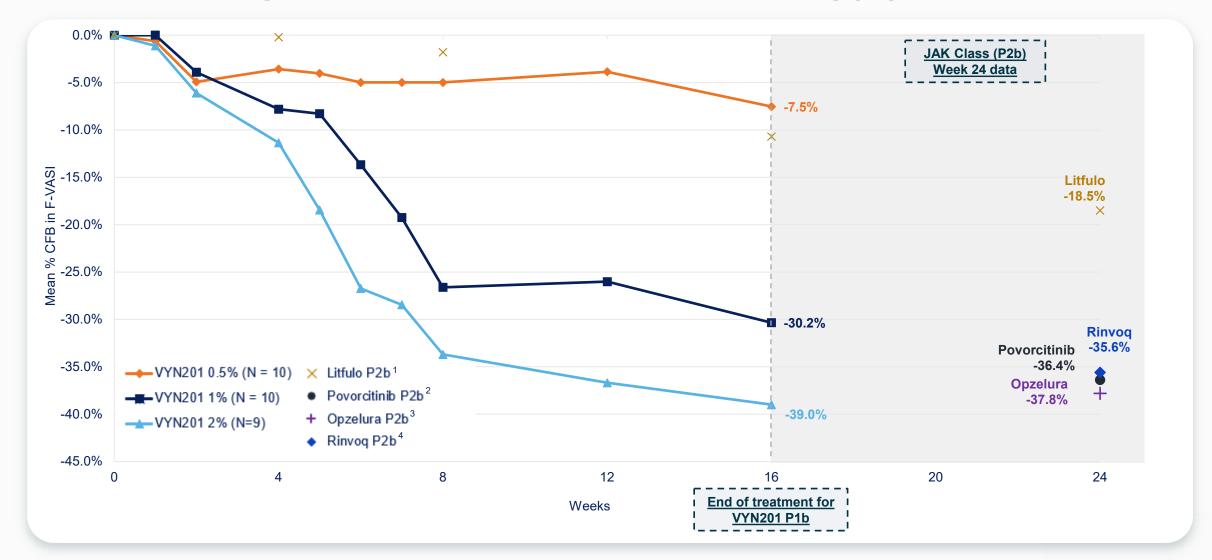
VYN201 Phase 1b: **QD Treatment in 100% active disease study population**





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

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



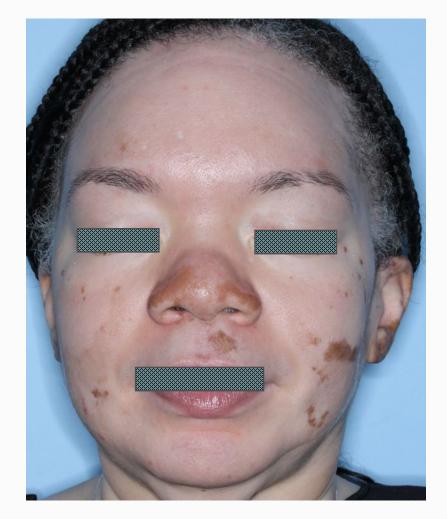
Note: Data is not based on Head-to-Head comparisons; Source: Clinicaltrials.gov; Study Publications: 1. NCT03715829 (LS mean %CFB for 50 mg QD); 2. NCT04818346 (LS mean %CFB for 45 mg QD); 3. NCT03099304 (LS mean %CFB for 1.5% BID); 4. NCT04927975 (LS mean %CFB for 11 mg QD);

Preclinical & Clinical Data Highlight Potential for Differentiated Product Profile

Characteristic	VYN201		Opzelura (Buvolitinih)	Litfulo (Bitlocitinib)	Povorcitinib	
Characteristic	1%	2%	(Ruxolitinib) Cream 1.5%	(Ritlecitinib) 50mg ¹	45mg²	
Novel MOA / JAK Class Alternative	✓		×	×	X	
Targeted Dosing Posology	QD		BID	QD	QD	
Rapid Onset of Action	✓		Moderate	X	Moderate	
Efficacy, % CFB F-VASI, Week 16	-30.2	-39.0	Active & stable disease study P2b: -37.8 (Week 24) ³	100% active disease study -1.8 (<u>Week 8</u>) -18.5 (<u>Week 24</u>)	Active & stable disease study -36.4 (Week 24)	
Efficacy, % F-VASI50, Week 12 ⁵	20.0	33.3	P2b: 21.2 ³ P3: 29.2 ⁴	0.0 (<u>Week 8</u>) 15.4 (<u>Week 24</u>)	25.0	
Potential to Upregulate WNT Pathway ⁶	\		X	X	X	
Safety Precaution	-		**Black Box"	*Black Box"	Expect "Black Box"	
Systemic Exposure	Low (Cmax <1 nM)		Cmax/AUC: 449nM / 3215nM	-	-	

Phase 1b Select Images

Subject with near-complete depigmentation (High FVASI)



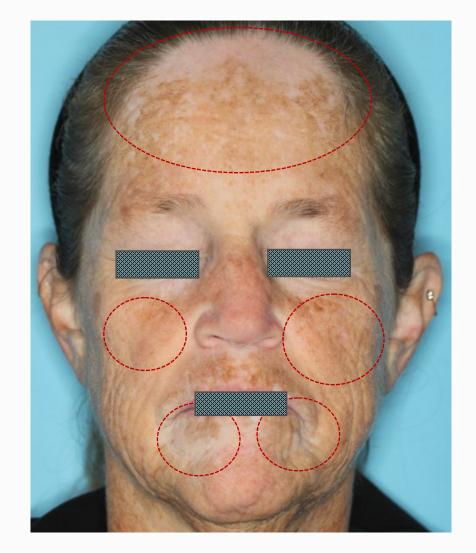


Baseline Week 16

(0.5% cohort, Fitzpatrick skin type: 5)

Phase 1b Select Images Subject with significant repigmentation response





Baseline

Week 16



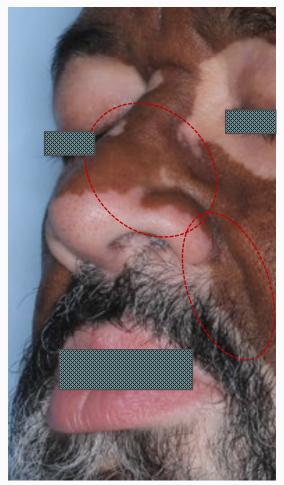
Phase 1b Select Images

Subject examples with marked active disease

Confetti-like depigmentation presentation

Inflamed vitiligo presentation







Baseline



Baseline Week 16

(1.0% cohort, Fitzpatrick skin type: 6)

(2.0% cohort, Fitzpatrick skin type: 5)

Week 16

Key Takeaways from VYN201 Phase 1b Results



- 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



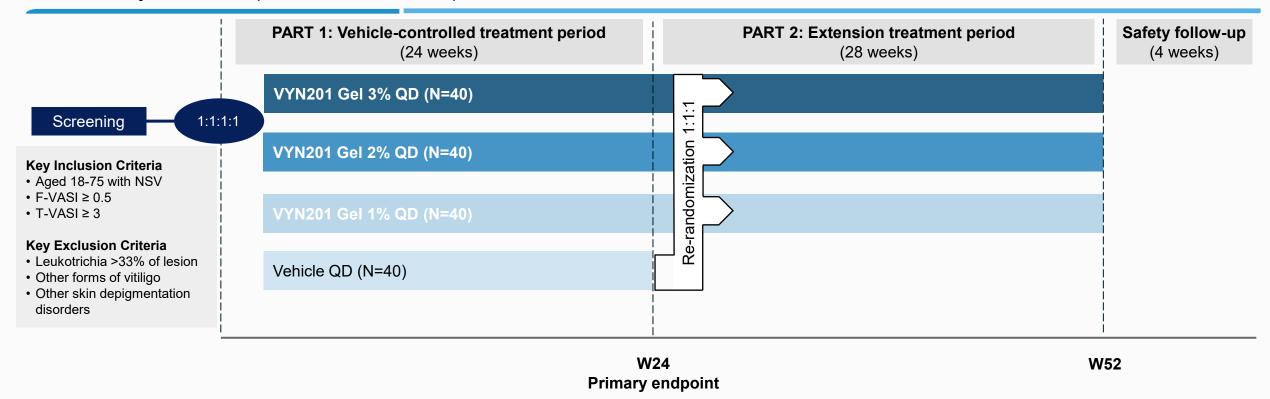
• Believed to be first clinical demonstration of BET inhibitor's effect in autoimmune disease¹



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

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

 $N = \sim 160$ subjects with NSV (active and stable disease)



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



VYNE's Drug Design Strategy

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

VYN201 Pan-BD BET Inhibitor

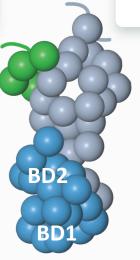
Maximize local effect & minimize systemic exposure

- 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

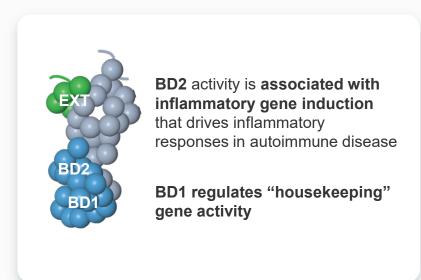
- Class-leading BD2 vs. BD1 selectivity for systemic administration
- BD2 activity more relevant to inflammatory gene expression
- Minimize BD1 inhibition to protect against steady-state gene disruption





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 development¹ which is designed to improve efficacy and tolerability





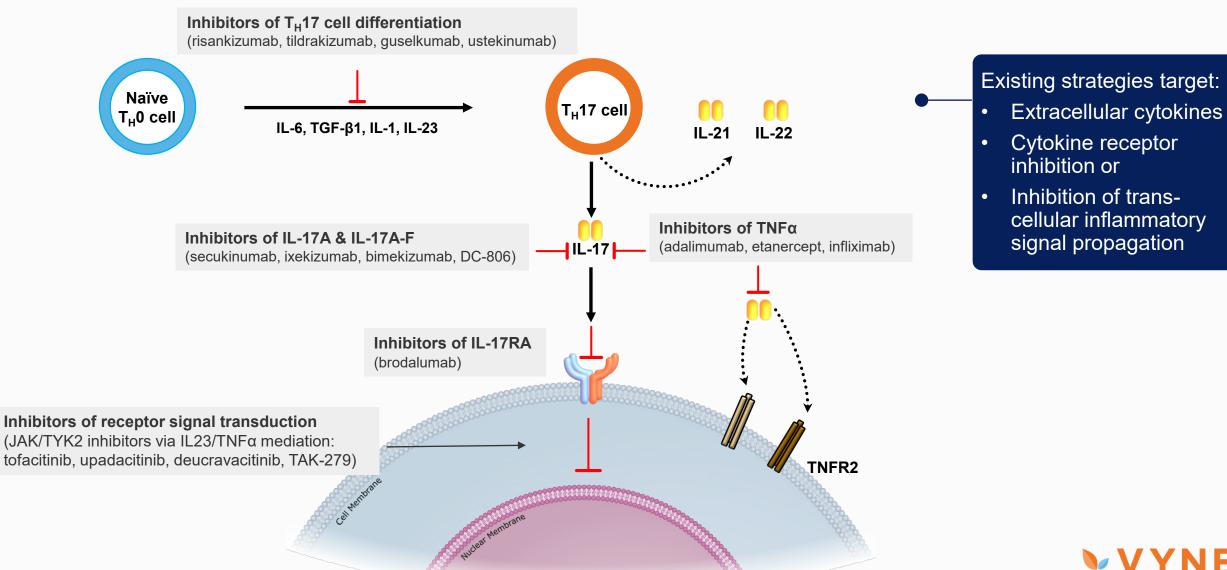
Compound ID	Potency vs. BD2* (nM)	Selectivity** (BD1/BD2)	
VYN202 (VYNE)	<	>>>>	
NUV-868 (Nuvation) ²	2	1,460x (FRET)	
ABBV-744 (AbbVie) ³	28	753x (FRET)	
GSK620 (GSK) ⁴	79	220x	
Pelabresib (Constellation) ²	17	5x (FRET)	
ABBV-075 ³	13	2.6x	
MK-8628/OTX-015 ⁵	26	1.5x	
BI-894999 ⁶	41	0.1x	

^{*}Lower number denotes higher potency

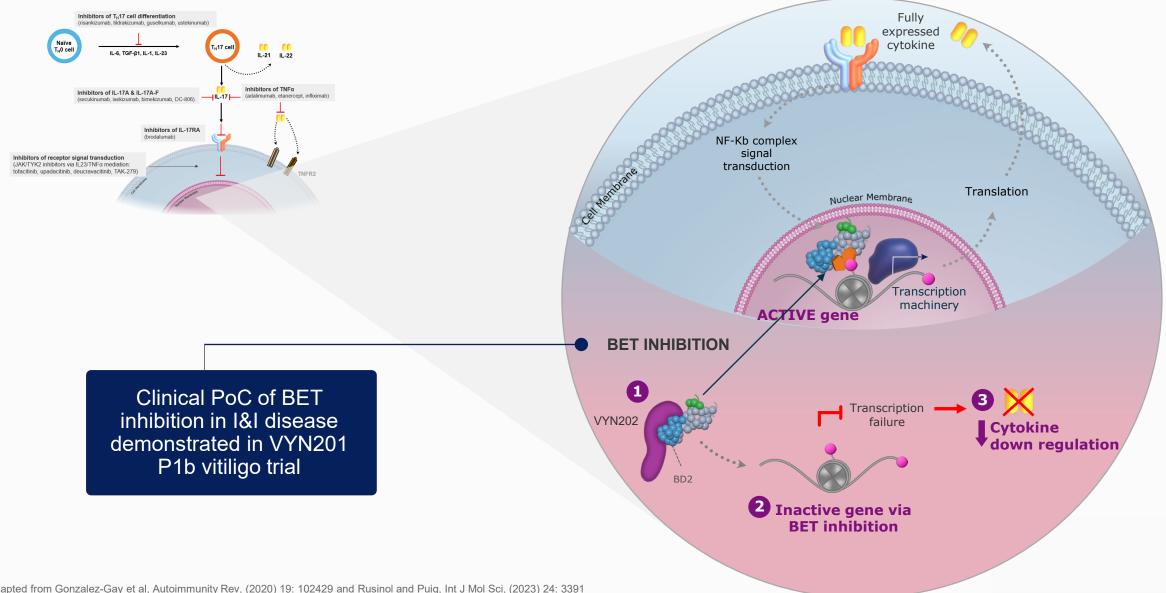
^{**}Higher number denotes higher selectivity. Data based on nanoBRET assay unless otherwise indicated.

^{1.} Based on readily available public information such as clintrials.gov, academic publications and corporate websites/presentations. 2. Nuvation corporate presentation (January 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

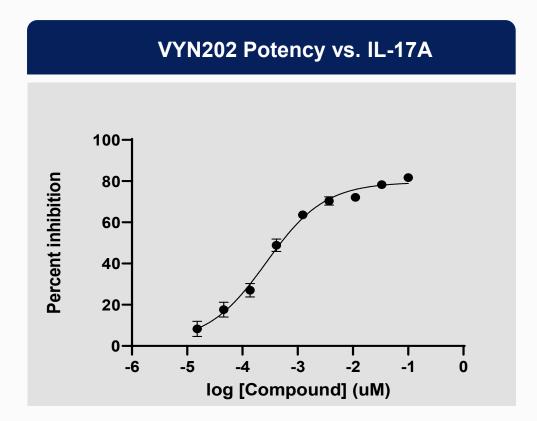


BET Inhibitors Disrupt Inflammatory Gene Transcription in T Cells to Directly Address the Complex Signaling of Immuno- & Fibro-inflammatory Diseases



Demonstrated Potency Against Th17 Cytokines

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





Therapeutic Agent	IC50 _{IL17A} (nM)
VYN202 (VYNE)	0.27
Secukinumab (Cosentyx - NVS):	0.37
DC-806 (DICE/LLY)	5.7



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	-



 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



Preclinical Efficacy Models



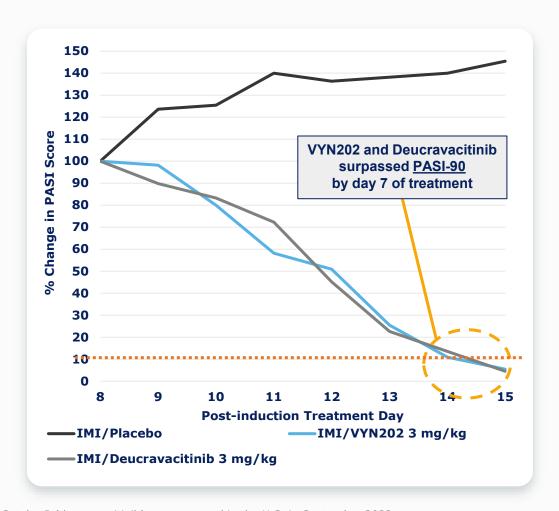
VYN202: Psoriasis Model

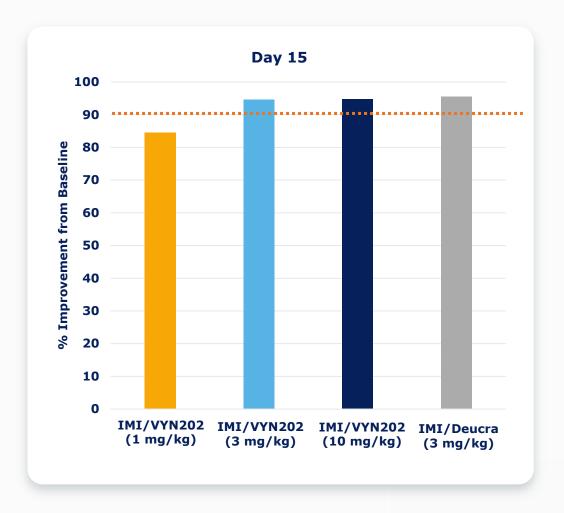


VYN202: Comparable Onset of Action and Efficacy to Deucravacitinib¹

at Equivalent Dosing in Preclinical in vivo Model of Psoriasis

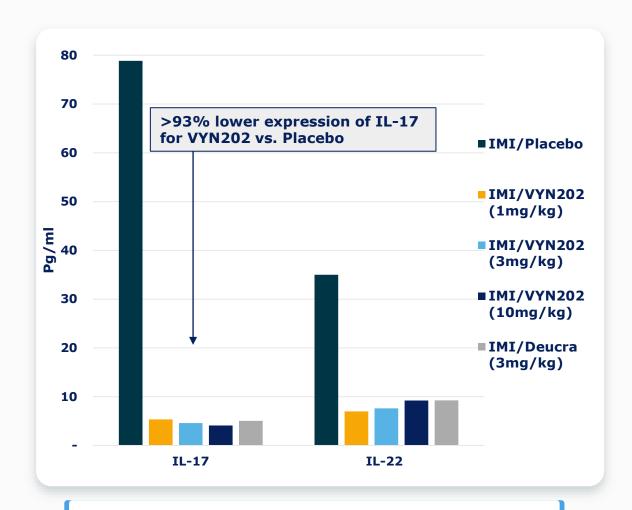
Dorsal depilated BALB-C mice were dosed for 14 days with topical imiquimod cream (Day 1-7: induction phase, Day 8-14: treatment phase). N=8 animals were assigned to each treatment group and received 3 mg/kg of allocated treatment intraperitoneally dosed once-daily on Day 8-14.

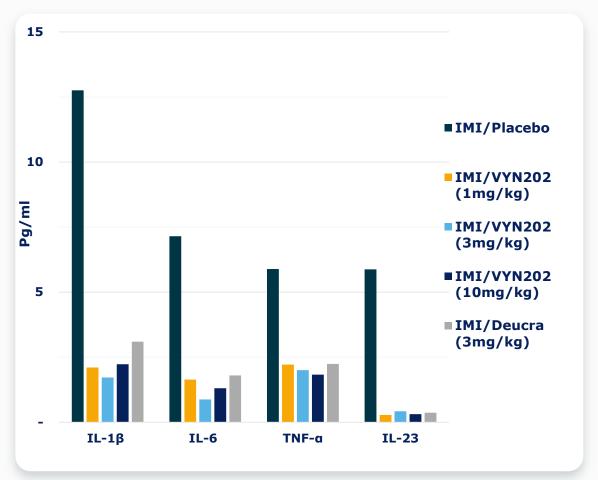




VYN202 Reduced Key Cytokines Associated with Pathogenesis of Psoriasis

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

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

Day 8
Before treatment







Day 15After 7 days of treatment





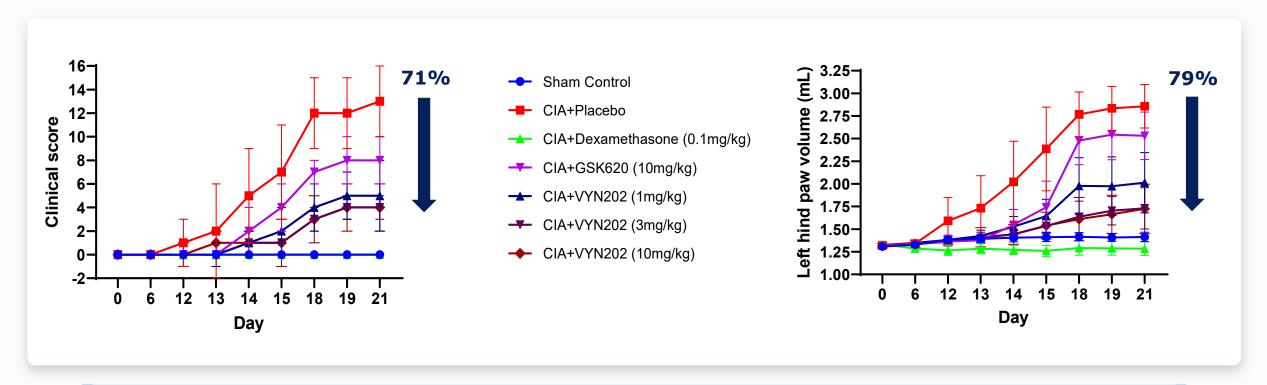


VYN202: Rheumatoid Arthritis Model



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

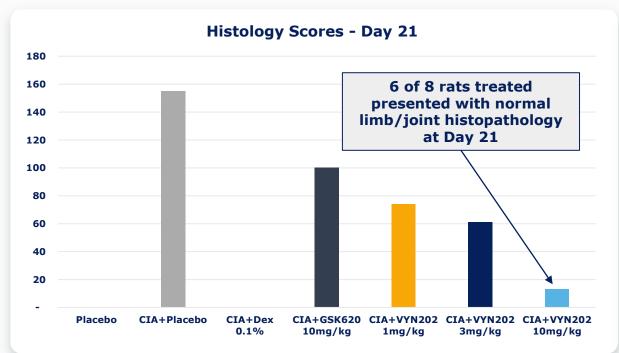


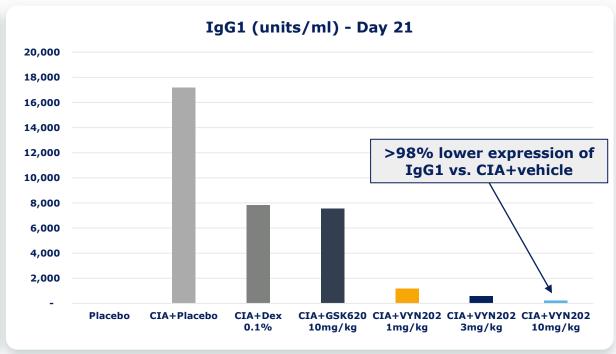
- VYN202 10mg/kg PO QD treatment resulted in a 71% lower clinical score and 79% lower paw volume compared to CIA+Placebo control at Day 21
- All VYN202 treatment groups were statistically significantly superior to both CIA+Placebo and GSK620 10mg/kg PO QD controls



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





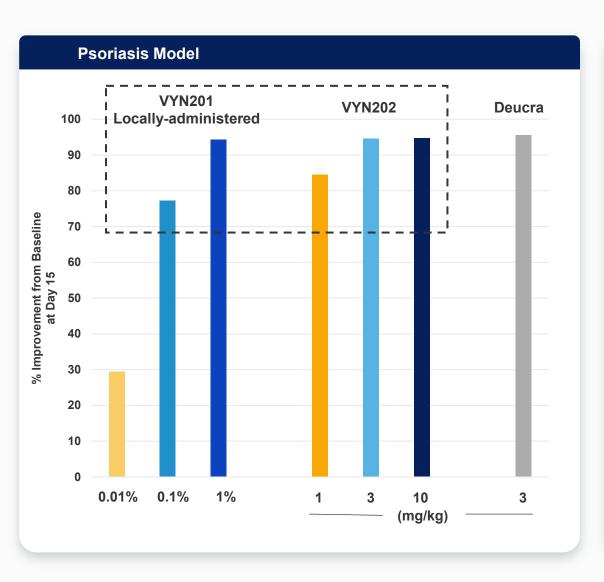
- CIA+VYN202 treatment resulted in a dose-dependent reduction in severity of arthritic histopathology & was statistically superior to CIA+Placebo and CIA+GSK620 at all doses
- VYN202 10mg/kg PO QD reduced the expression of IgG1 by >98% vs. CIA+Placebo control & was statistically equivalent to Placebo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

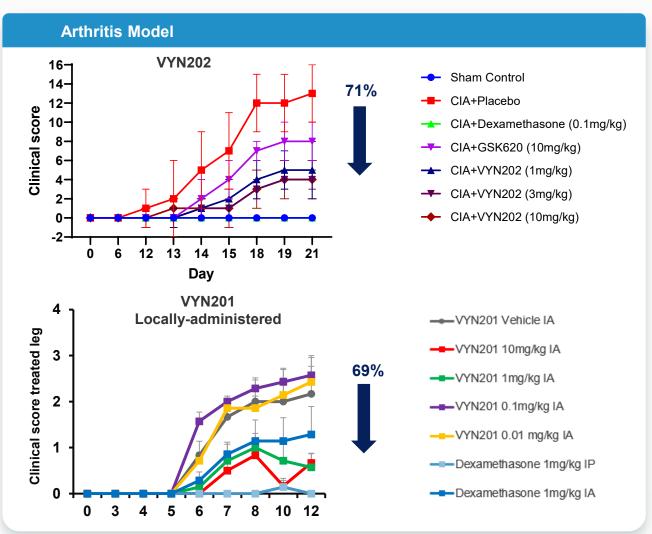


^{*}Immunoglobin G1

VYN202 Results Show Strong Correlation with VYN201 Results

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





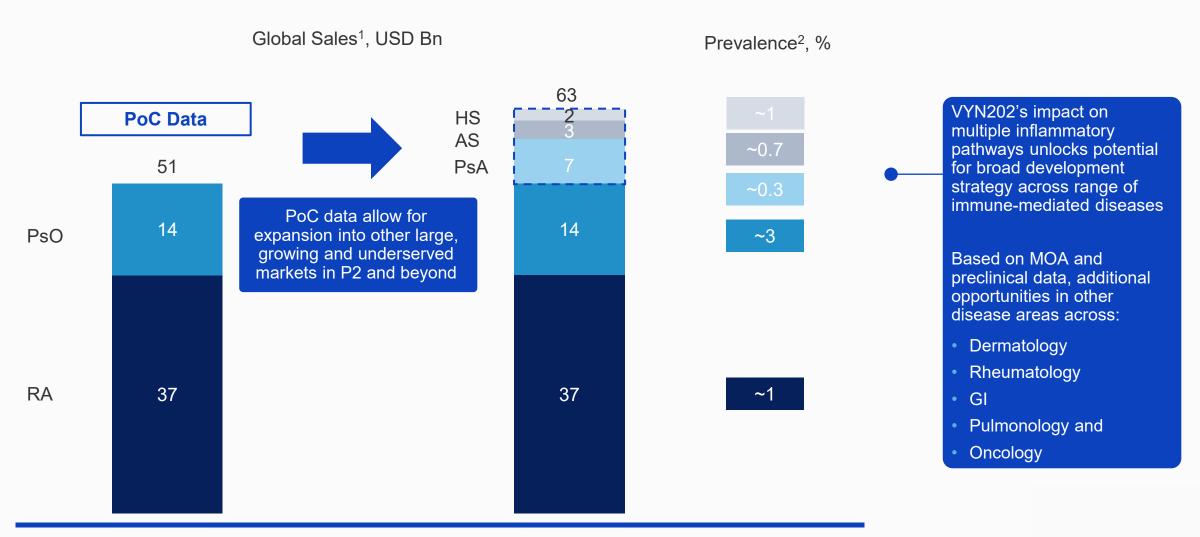
VYN202 Clinical Development Plan

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



Clinical Development Strategy

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



VYN202 Planned Study Designs



Healthy Volunteers



PoC Studies in Patients with Disease

SAD



MAD



Psoriasis (Mod/Severe)



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

Trial size: N=~40 Evaluating 5 strengths of VYN202 (N=8 / cohort) and food effect



- 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

P1 SAD/MAD expected to be initiated in Q2 2024 with results anticipated 2H 2024

- Multicenter, double-blind, placebocontrolled 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 moderateto-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, placebocontrolled 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

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



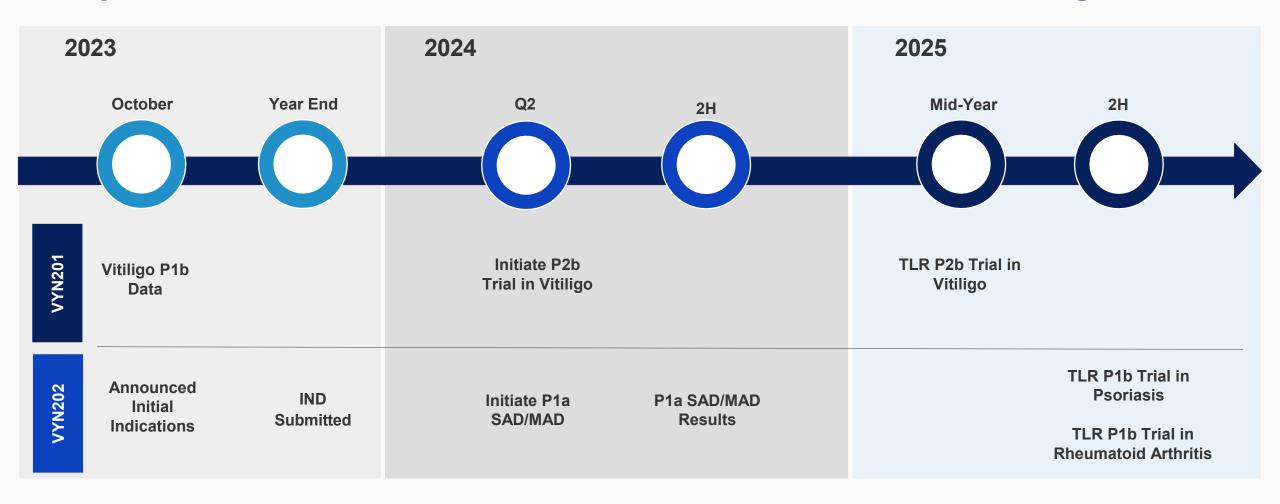
 Strong preclinical data across multiple diverse models of autoimmune disease demonstrating significant down regulation of key pro-inflammatory & disease-related biomarkers with corresponding improvements in disease severity



• 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



Cash runway through the end of 2025



Appendix



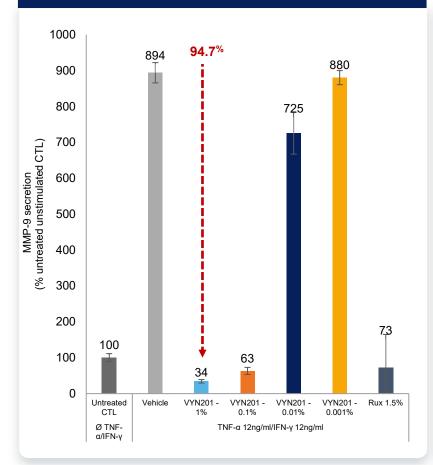
VYN201: Preclinical Data



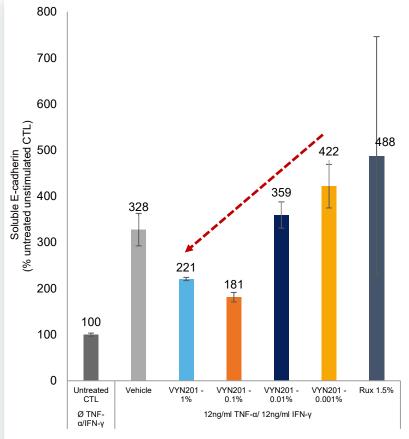
VYN201: Human Tissue Model of Vitiligo

Demonstrated reduction in melanocyte loss and lowering of key inflammatory biomarkers

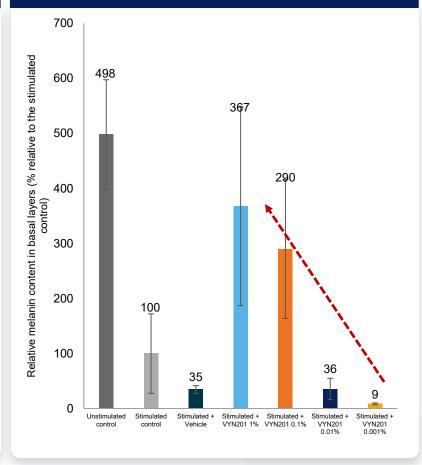
VYN201 1% **reduced the secretion of MMP9** relative to stimulated vehicle, and numerically superior to ruxolitinib 1.5%



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



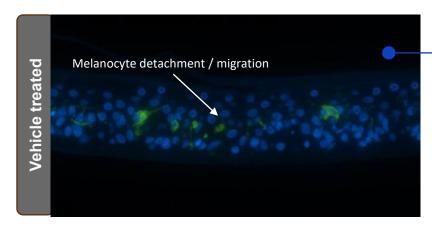
VYN201 substantially prevents the loss of melanin pigment in the basal layers of skin in a dose dependent manner



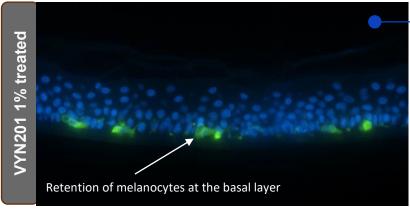
Reconstituted human epithelial (RHE) skin cultures were treated with a TNF-a and IFN-y cytokine cocktail to induce a vitiligo phenotype melanocytorrhagy (loss of melanocyte), upregulation of MMP9 and soluble E-cadherin).

VYN201: Human Tissue Model of Vitiligo

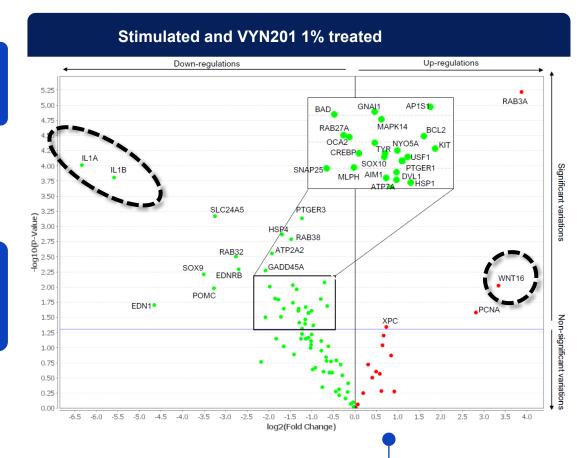
VYN201 prevents melanocyte detachment, down regulates the expression of key cytokines and upregulates WNT pathway



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)

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

VYN201: Phase 1 Proof-of-Concept

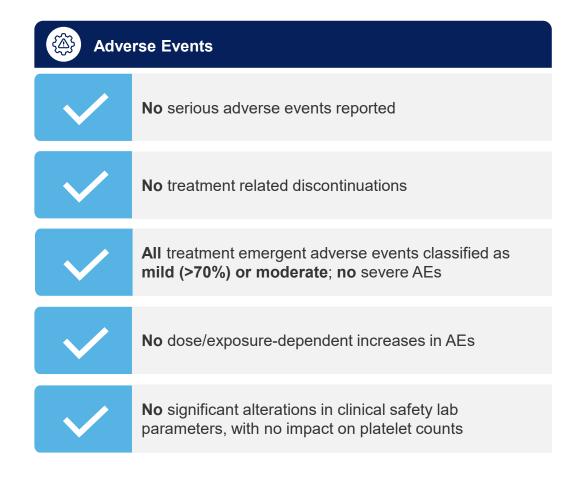


Baseline Demographic and Clinical Characteristics

†	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. / %								
T 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



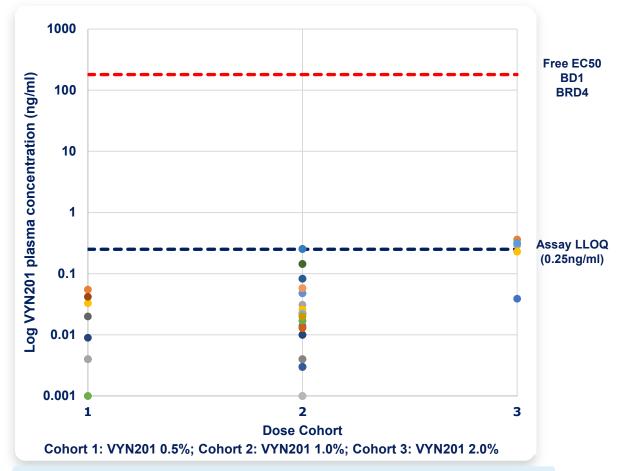


Assessment	Mean Score Range 0 (None) to 3 (Severe)				
Burning/Stinging	0.26				
Scaling	0.15				
Dryness	0.22				
Pruritus	0.14				
Erythema	0.29				
Hyperpigmentation	0.10				

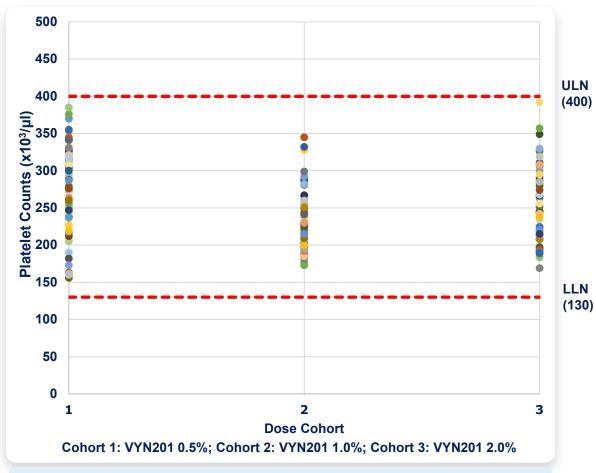


VYN201 Phase 1b: Low Systemic Exposure in Vitiligo Subjects Correlates with No Impact on Platelet Counts

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



- 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)