VYNE™ THERAPEUTICS

INVESTOR PRESENTATION

August 2023

ROOTED IN INNOVATION

Forward Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 including, but not limited to, statements regarding preclinical and clinical development and timelines for VYNE's BET inhibitor platform, VYNE's ability to fund its operations through the end of 2023, and other statements regarding the future expectations, plans and prospects of VYNE. All statements in this presentation which are not historical facts are forward-looking statements. Any forward-looking statements are based on VYNE's current knowledge and its present beliefs and expectations regarding possible future events and are subject to risks, uncertainties and assumptions that could cause actual results to differ materially and adversely from those set forth or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: VYNE's ability to successfully develop its product candidates; the timing of commencement of future preclinical studies and clinical trials and the receipt of results in such studies and trials; VYNE's ability to enroll patients and successfully progress, complete, and receive favorable results in, clinical trials for its product candidates; VYNE's intentions and its ability to obtain additional funding, either through equity or debt financing transactions or collaboration arrangements; disruptions related to COVID-19 or another pandemic, epidemic or outbreak of a contagious disease, on the ability of VYNE's suppliers to manufacture and provide materials for VYNE's product candidates, initiating and retaining patients in clinical trials, operating results, liquidity and financial condition; the regulatory approval process for VYNE's product candidates, including any delay or failure in obtaining requisite approvals; the potential market size of treatments for any diseases and market adoption of products, if approved or cleared for commercial use, by physicians and patients; developments and projections relating to competitors and the pharmaceuticals industry, including competing drugs and therapies; the timing or likelihood of regulatory filings and approvals or clearances for product candidates; VYNE's ability to comply with various regulations applicable to its business; VYNE's ability to create intellectual property and the scope of protection it is able to establish and maintain for intellectual property rights covering its product candidates, including the projected terms of patent protection; risks that any of VYNE's patents may be held to be narrowed, invalid or unenforceable or one or more of VYNE's patent applications may not be granted and potential competitors may also seek to design around VYNE's granted patents or patent applications; the timing, costs or results of litigation, including litigation to protect its intellectual property; VYNE's ability to successfully challenge intellectual property claimed by others; estimates of VYNE's cash runway, expenses, capital requirements, its needs for additional financing and its ability to obtain additional capital on acceptable terms or at all; VYNE's ability to attract and retain key scientific or management personnel; VYNE's defense of any litigation that may be initiated against it; VYNE's expectations regarding licensing, business transactions and strategic operations; VYNE's future financial performance and liquidity; and volatility in VYNE's stock price may result in rapid and substantial increases or decreases in the stock price that may or may not be related to VYNE's operating performance or prospects. For a discussion of other risks and uncertainties, and other important factors, any of which could cause VYNE's actual results to differ from those contained in the forward-looking statements, see the section titled "Risk Factors" in VYNE's Annual Report on Form 10-K for the year ended December 31, 2022 and Quarterly Report on Form 10-Q for the period ended June 30, 2023, as well as discussions of potential risks, uncertainties, and other important factors in VYNE's subsequent filings with the U.S. Securities and Exchange Commission. Although VYNE believes these forward-looking statements are reasonable, they speak only as of the date of this presentation and VYNE undertakes no obligation to update publicly such forward-looking statements to reflect subsequent events or circumstances, except as otherwise required by law. Given these risks and uncertainties, you should not rely upon forward-looking statements as predictions of future events.

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

Multiple paths to potential value creation and catalysts

Program	Potential Indication(s)	Route of Administration	Current Stage			Anticipated Milestones & Recent Updates	Rights
			Preclinical	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 1a completed • Q3 2023: Preliminary Phase 1b safety and efficacy data • Oct. 2023: Final Phase 1b safety and efficacy data	Worldwide
	Those benefiting from local administration, "soft drug" approach, and anti-fibrotic activity such as rheumatology and lung disease	Inhaled / Injectable				• 2023: Selection of 2nd indication	Worldwide
VYN202 BD2-selective BET inhibitor	I&I such as RA, psoriasis, systemic lupus erythematosus, UC/Crohn's and MS[1]	Oral				• IND-enabling studies ongoing • Q4 2023: Selection of indication • Q4 2023: Submit IND	Worldwide

Note: Cash runway guidance through the end of 2023 assumes development activities for VYN201 in nonsegmental vitiligo and continued advancement of VYN202, based on current estimates. Refer to slide 2 "Forward Looking Statements" for description of risks and uncertainties regarding the future expectations, plans and prospects of VYNE. Subject to adequate levels of funding. 1. List included is illustrative and not exhaustive and subject to completion of requisite pre-clinical evaluations.

BET = Bromodomain and extra-terminal protein

InhiBET™ BET Inhibitor Platform

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

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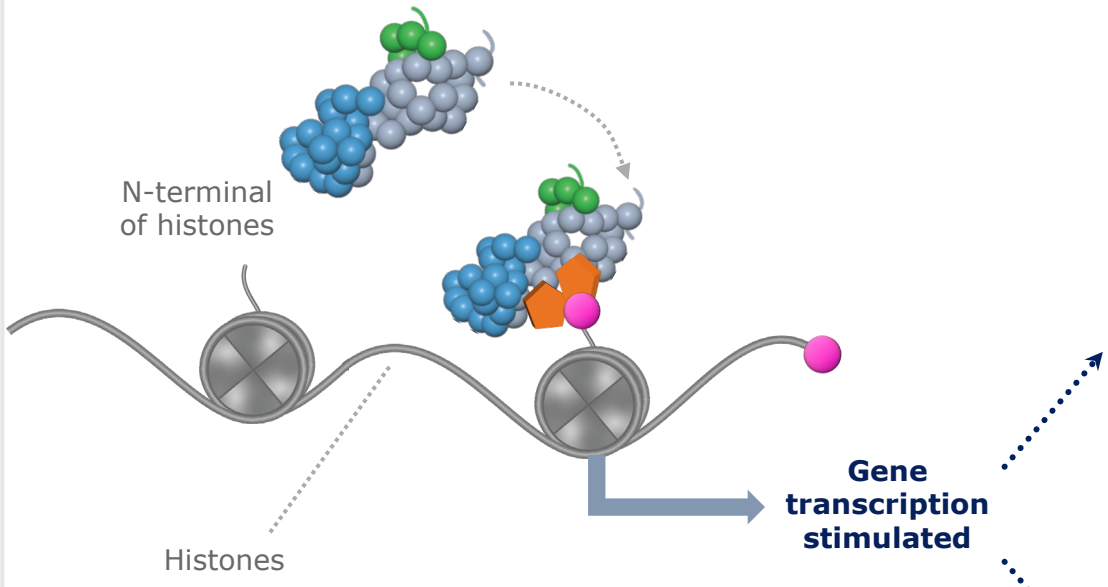
BET Proteins Play a Key Role
in the Regulation of Inflammatory and Oncogenic Genes involved in Several Diseases



BET proteins "read" acetylated lysines and enable transcription of:

Pro-inflammatory genes, leading to:

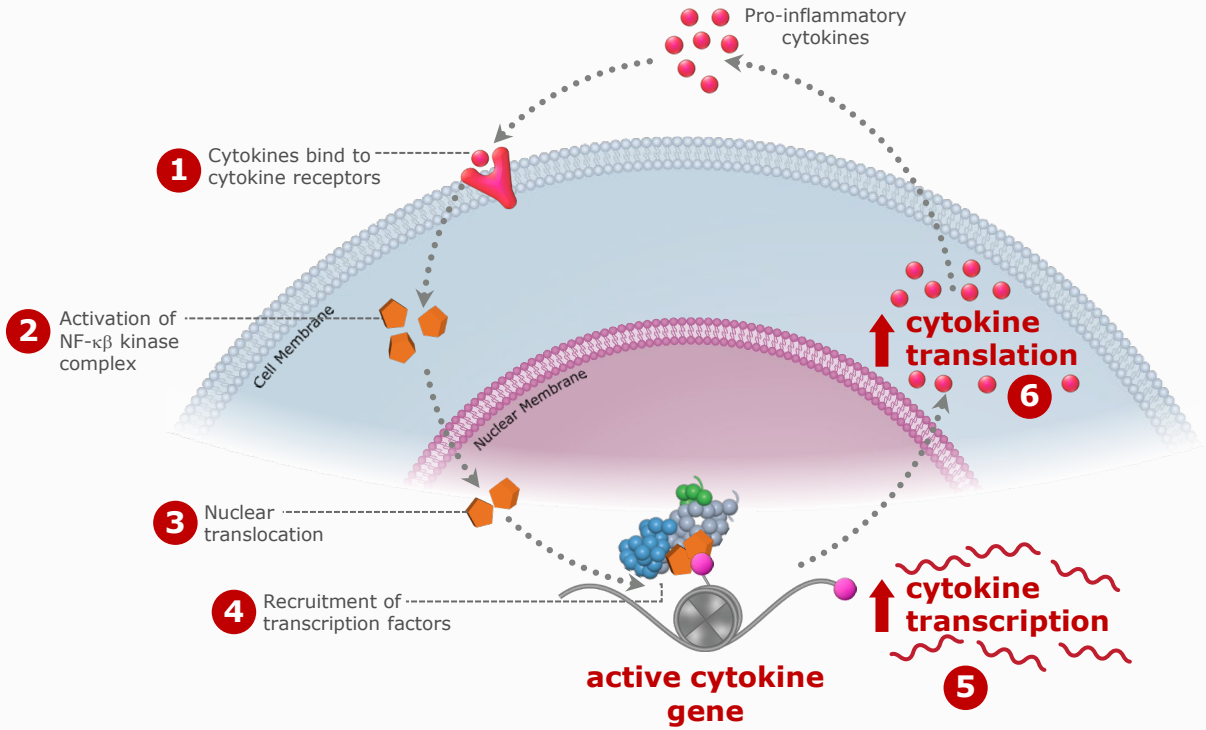
- Increased cytokine expression that activate B&T cells
- An increase in autoimmune and cardiovascular diseases

Oncogenic genes, leading to:

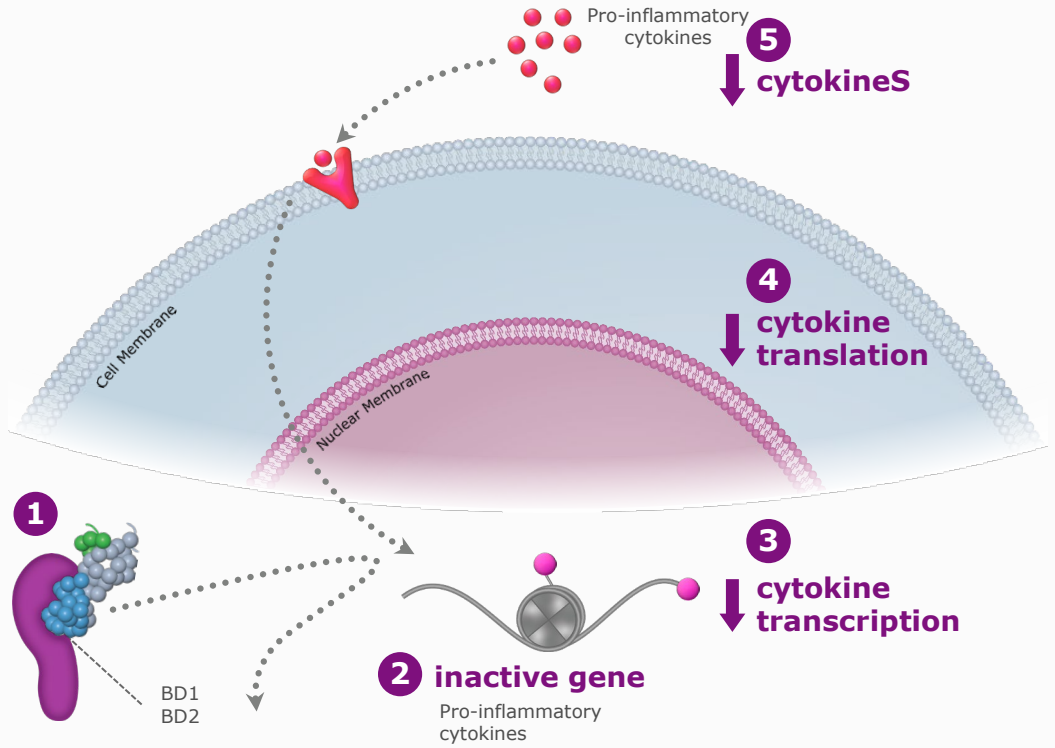
- Increased cell proliferation/survival
- An increase in solid tumors and hematologic malignancies

BET Inhibitors Stall the "Vicious Cycle"
of Pro-Inflammatory Cytokine Production in Autoimmune Diseases

Pro-Inflammatory Cytokine Production



BET Inhibition

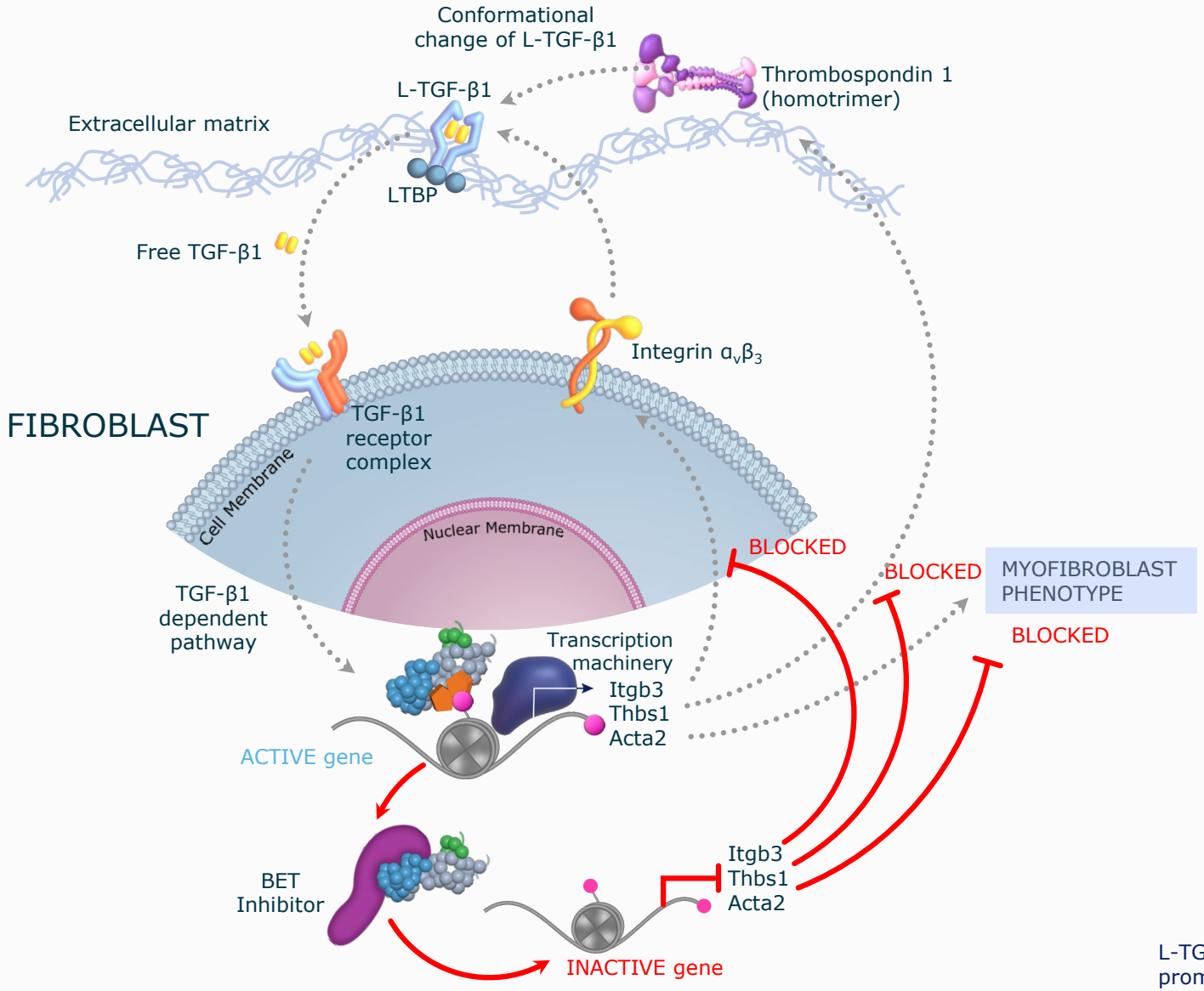


BET INHIBITOR

Binds to BD1 and/or BD2 binding domains of BET protein making it unable recognize acetylated histones, recruit transcription factors and release pro-inflammatory cytokines

NF-κB = Nuclear Factor Kappa B

BET Inhibition May Reduce TGF-b1 Expression and Myofibroblast Phenotype



- Myofibroblasts are activated in response to tissue injury to repair lost or damaged extracellular matrix
- Enhanced collagen secretion and subsequent scarring are part of the normal wound healing response
- Due to myofibroblasts ability to repair but not regenerate, accumulation of scar tissue is always associated with reduced organ performance
- BET inhibition may reduce TGF-b1 expression and related myofibroblast phenotype

L-TGFb1 – Latent TGF-b1; Thbs1 – Thrombospondin 1 promoter; Itgb3 - Integrin beta 3 promoter; Acta2/a-SMA – Biomarker for myofibroblast formation

Kawahito et al, Pulm. Pharma & Therp, 2021, 70:102057

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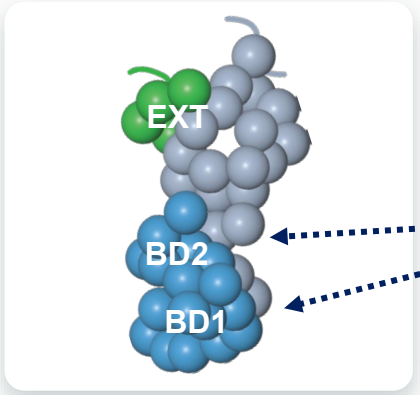
BD1 and BD2 Play Different Roles in Regulating Gene Expression

Maximizing on-target potency against BD2 and minimizing affinity to BD1 may be the key to optimizing the benefit/risk profile of systemic BET inhibitors for autoimmune diseases



BET proteins are characterized by **2 bromodomains** (BD1 and BD2) and **1 extra-terminal domain**

BD1 and BD2 domains **are recognized as druggable targets** but **play different roles in gene regulation**

BD1 and BD2 role differentiation:

Characteristic	BD1	BD2
Key to steady-state gene regulation?	Yes	No
Key to inflammatory gene induction?	No	Yes
Anti-inflammatory effect via selective antagonism?	No	Yes
GI and hematological toxicities via selective antagonism?	Yes	No

BD1 regulates "housekeeping" gene activity. BD1 inhibition via systemic administration has been linked to potential clinical safety findings including GI toxicity and thrombocytopenia

BD2 BET activity is associated with inflammatory gene induction that drives inflammatory responses in autoimmune disease

Gilan et al, Science. 2020 April 24; 368(6489): 387–394; Shi & Vakoc, *Mol. Cell* 2014

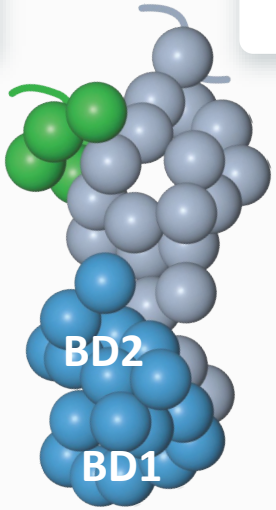
VYNE's Drug Design Strategy

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

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VYN201
Locally administered pan-BET inhibitor

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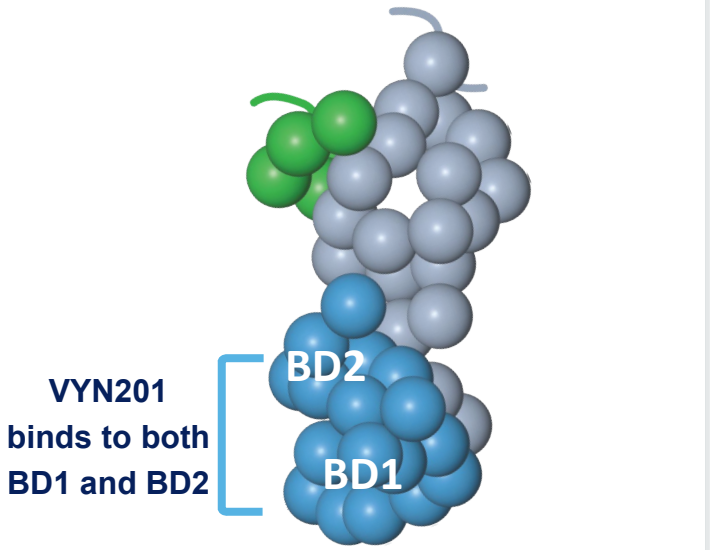
VYN201 – Locally Administered Pan-BD BET Inhibitor

Designed as a "soft" drug for tissue targeted administration to maximize local effect and minimize systemic exposure

BET Protein



Potential Target Market:

- Vitiligo
- Other indications benefiting from local administration and "soft drug" approach

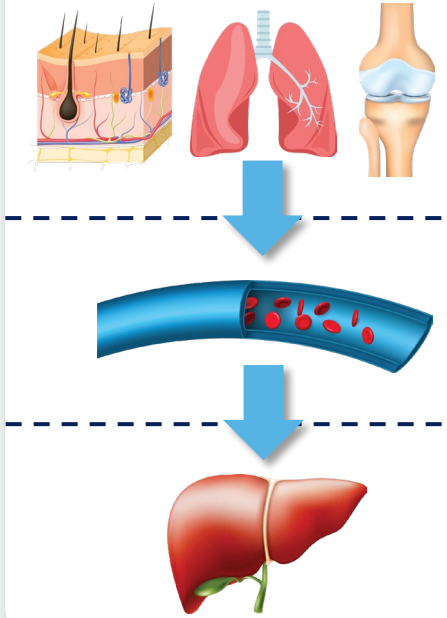
Broad activity:

- Binds to BD1 and BD2 domains (pan-BD)

Targeted Near Term Milestones:

- Q3 2023: Preliminary Phase 1b safety and efficacy data
- October 2023: Final Phase 1b safety and efficacy data

Soft Drug Design



TLR = Top Line Results

VYN201: Why Local Administration and "Soft"?

Systemic administration of pan-BD BET inhibitors has been linked to potential clinical safety findings including GI toxicity and thrombocytopenia

First-in-Human of *oral pan-BD* BET inhibitor ABBV-075 in Patients with Relapsed/ Refractory Solid Tumors

	Dose escalation ($n = 72$)		Prostate expansion ($n = 12$)		All patients ($n = 84$)	
n (%)	All grades	Grade 3/4	All grades	Grade 3/4	All grades	Grade 3/4
AE in >20% of all patients[a]	70 (97)	52 (72)	11 (92)	10 (83)	81 (96)	62 (74)
Thrombocytopenia	38 (53)	24 (33)	5 (42)	5 (42)	43 (51)	29 (35)
Dysgeusia	36 (50)	2 (3)	5 (42)	0	41 (49)	2 (2)
Fatigue	29 (40)	3 (4)	7 (58)	2 (17)	36 (43)	5 (6)
Nausea	25 (35)	1 (1)	5 (42)	1 (8)	30 (36)	2 (2)
Decreased appetite	20 (28)	3 (4)	5 (42)	0	25 (30)	3 (4)
Anemia	19 (26)	13 (18)	4 (33)	3 (25)	23 (27)	16 (19)
Diarrhea	18 (25)	4 (6)	3 (25)	0	21 (25)	4 (5)
Vomiting	17 (23)	1 (1)	3 (25)	0	20 (24)	1 (1)
Dyspnea	14 (19)	7 (10)	4 (33)	0	18 (21)	7 (8)
AE related to	64 (89)	40 (56)	10 (83)	8 (67)	74 (88)	48 (57)

VYN201 is designed to addresses potential systemic toxicities through:

Localized drug delivery strategy
(tissue specific - e.g., skin, lung, joint)

Soft drug approach
hepatic clearance /
high first pass metabolism via liver

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Faivre et al, Nature, 578, February 2020; Piho-Paul et al, Clin Cancer Res, 25(21), November 2019

VYN201 Pre-Clinical Efficacy Model Evaluations

Program designed to investigate the targeted administration of a "soft drug" pan-BD BET inhibitor to maximize local effect and minimize systemic exposure

Indication/area	Model	Administration Route	Status
Th17 autoimmune diseases	IMI-induction mouse model	Topical	Complete
Th2 autoimmune diseases	DNCB-induction mouse model	Topical	Complete
Fibrosis	Wound healing outcomes mouse model	Topical	Complete
Vitiligo	Reconstituted human epithelial skin TNFα/IFNγ induction model	Topical	Complete
Idiopathic pulmonary fibrosis	Bleomycin-induction mouse model	Intra-nasal	Complete
Rheumatoid arthritis	Intra-articular cytokine cocktail mouse model	Intra-articular	Complete
Macular degeneration	Choroidal neovascularization rat model	Intra-orbital/vitreous	Complete
Colitis (gut restricted)	DSS-induction mouse model	Oral	Complete
Oncology (AML/melanoma)	Human cell line screening and biomarker discovery	In-vitro	On-going

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VYN201: Preclinical Proof-of-Concept Data Summary

Potential "pipeline in a product" with broad utility across multiple routes of administration

Preclinical models produced consistent reductions in pro-inflammatory & disease-related biomarkers, improvements in disease severity and a demonstrated local activity

Vitiligo Model (Topical)

- Highest doses demonstrated statistically significant improvement in reducing melanocyte loss & lowering key inflammatory biomarkers MMP9 and soluble e-cadherin vs. vehicle
- Numerically superior to active control, ruxolitinib cream, 1.5%

TH17 Inflammation Model (Topical)

- Significantly reduced expression of several key pro-inflammatory proteins relevant to Th17-mediated autoimmune diseases in human tissue
- Reduced composite score of inflammation severity

IPF[1] & Fibrotic Tissue Models (Inhaled and Topical)

- Significantly lower fibrosis vs. vehicle and negative control
- Preliminary IPF model data suggests VYN201 could have promising impact on IPF-related fibrosis and biomarkers

Arthritis Model (Intra-articular Injection)

- Two highest doses produced statistically significant improvement in treatment response
- Demonstrated localized dose-dependent effect

1. Idiopathic pulmonary Fibrosis (IPF)
2. Data on file

VYN201: Vitiligo
Preclinical data and Clinical Plan

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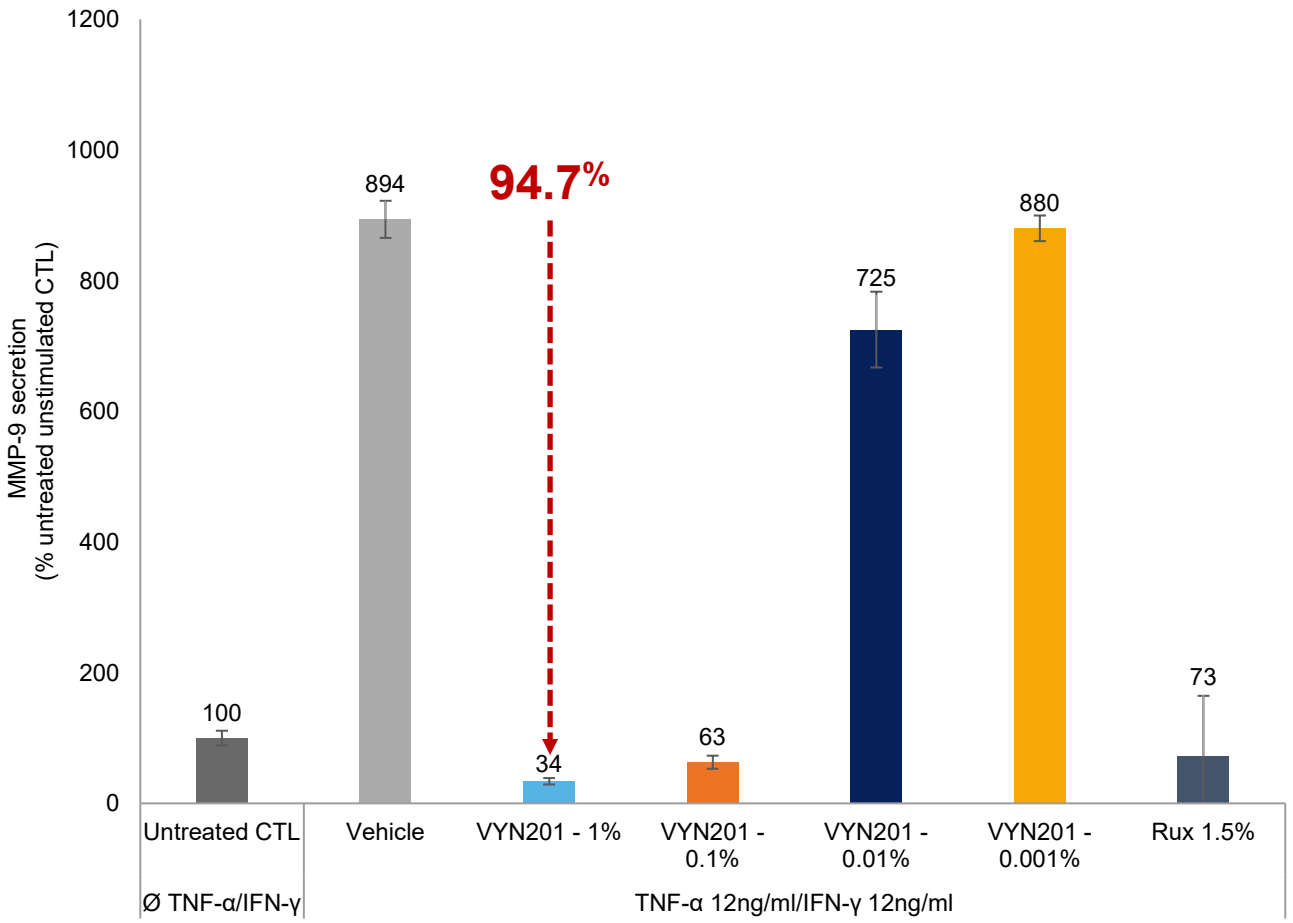
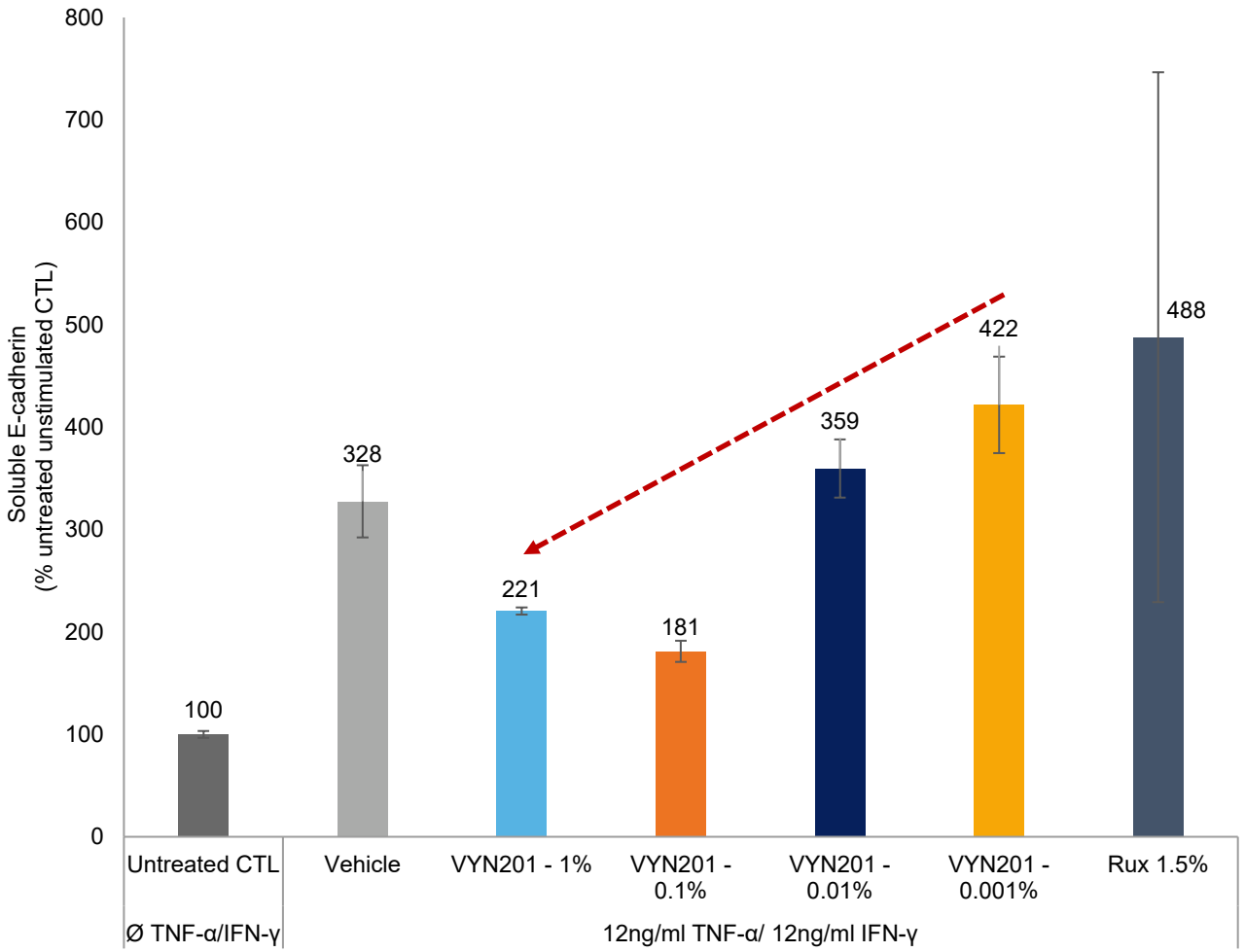
VYN201: Human Tissue Model of Vitiligo – Demonstrated Inhibition of MMP9

Reconstituted human epithelial (RHE) skin cultures were treated with a TNF-α and IFN-γ cytokine cocktail to induce a vitiligo phenotype melanocytorrhagy (loss of melanocyte), upregulation of MMP9 and soluble E-cadherin). 24hr prior to stimulation, RHE samples were topically treatment with VYN201 at varying concentrations and topical ruxolitinib 1.5% cream at 3 mg/cm^2



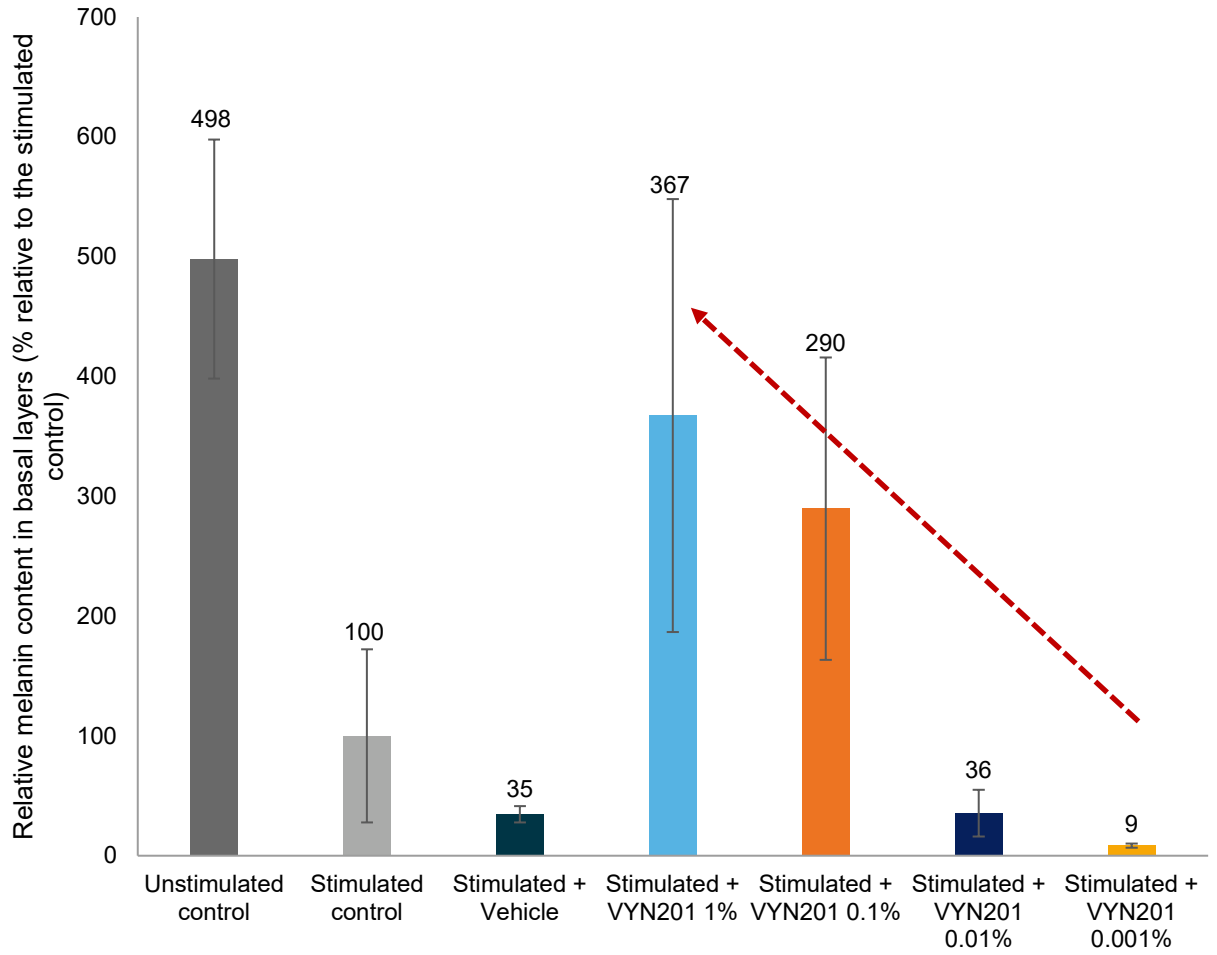
- Stimulated and vehicle treated RHE demonstrated a significant upregulation of MMP9, relative to unstimulated and untreated control
- VYN201 markedly reduced the expression of MMP9 in a dose-dependent manner with a maximal effect at the 1% concentration
- VYN201 1% reduced the secretion of MMP9 by 94.7%, relative to stimulated vehicle, and numerically superior to ruxolitinib 1.5%

VYN201: Human Tissue Model of Vitiligo – Reduction of Soluble E-cadherin



- Stimulated and vehicle-treated RHE demonstrated a significant upregulation of soluble E-cadherin, relative to unstimulated control
- **VYN201 affects a dose-dependent reduction in solubilized E-cadherin**
- VYN201 was numerically superior to topical ruxolitinib cream 1.5%

VYN201: Human Tissue Model of Vitiligo – Effect on Melanocyte Retention

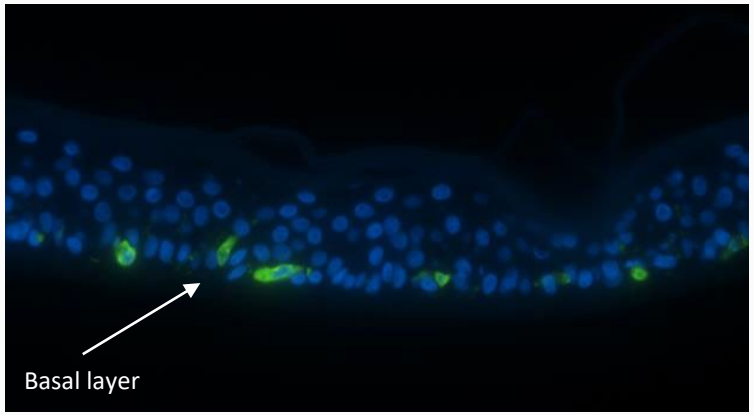


- Stimulated and vehicle-treated RHE demonstrated a significant loss in melanin content, relative to unstimulated control
- **VYN201 substantially prevents the loss of melanin pigment in the basal layers of skin in a dose dependent manner**
- Residual melanin levels for VYN201 1% was approximately 10-fold higher than vehicle, retaining approximately 75% of melanin relative to unstimulated control

Note: Melanin content in skin cultures treated with ruxolitinib 1.5% cream was immeasurable due to tissue intolerance to treatment

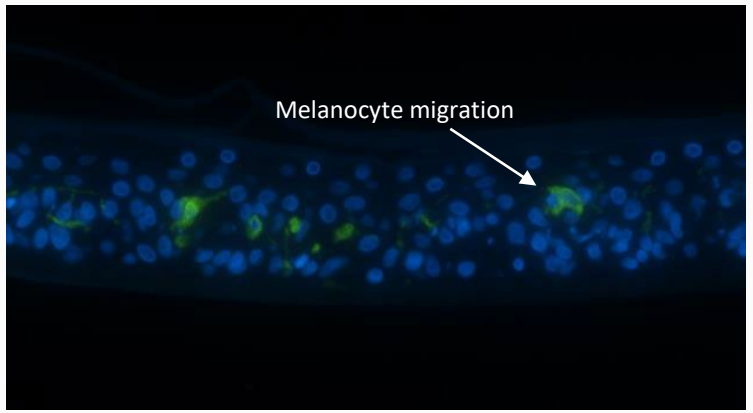
VYN201: Human Tissue Model of Vitiligo - Histology

Micrographic images of TRV immuno-stained induced RHE specimens demonstrating the preservation of melanocytes in the basal layer of samples treated with VYN201 1%



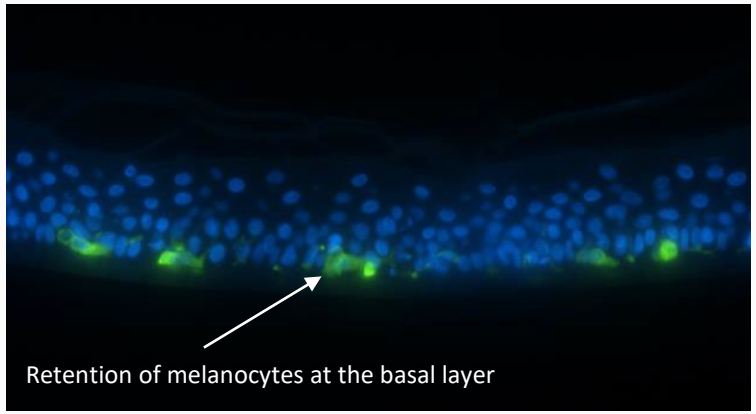
Unstimulated and untreated control

Melanocytes remain at or close to the basal layer implying that E-cadherin adhesion is still functional



Stimulated and Vehicle treated

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



Stimulated and VYN201 1% treated

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

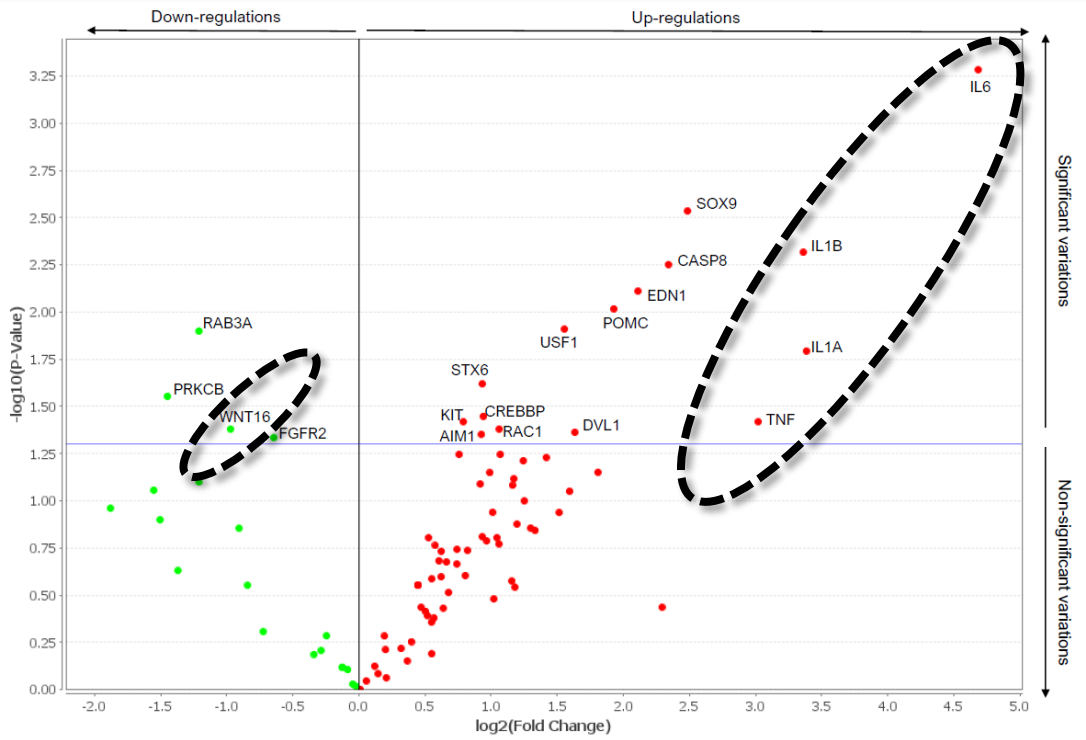
Keratinocytes (blue), melanocytes (green)

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

VYN201: Human Tissue Model of Vitiligo – Gene regulation

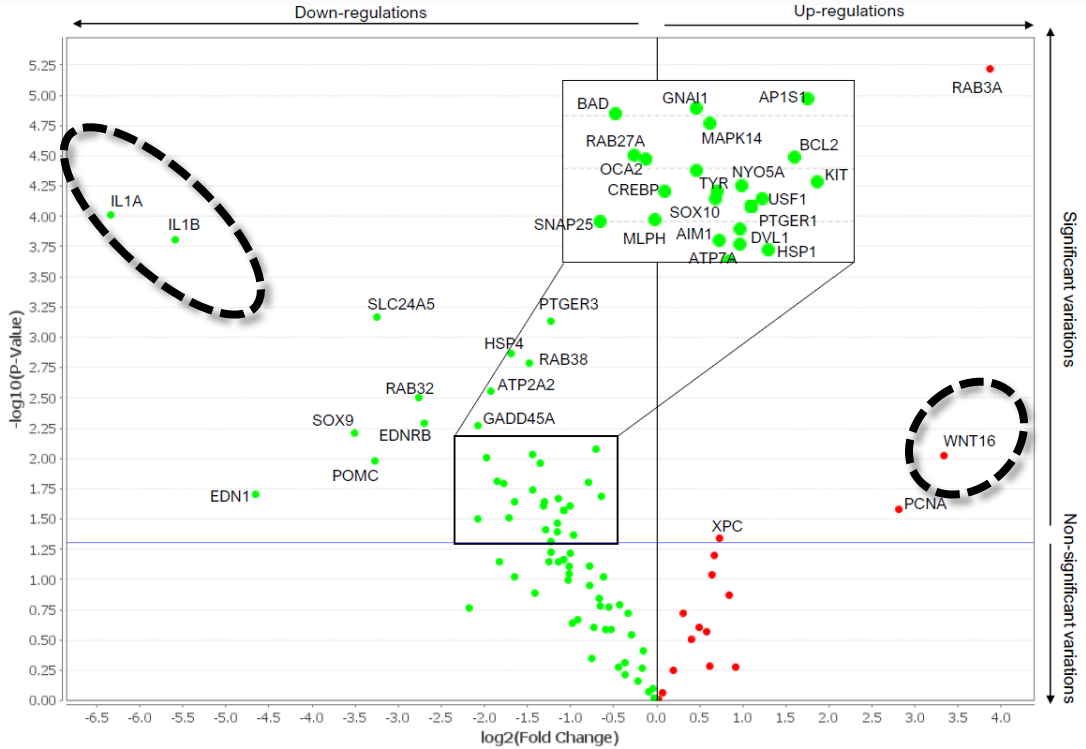
Preliminary data suggest that VYN201 regulates genes relevant to Vitiligo including impacting WNT pathway which is believed to play a key role in melanocyte regeneration

Transcriptome volcano plots of genes relevant to vitiligo (preliminary findings):



Stimulated control

Significant upregulation of cytokines IL6, IL1A and IL1B and TNF



Stimulated and VYN201 1% treated

Significant downregulation of cytokines IL6, IL1A and IL1B and TNF and upregulation of the WNT pathway IL6 and TNF downregulated below LLOQ of assay

LLOQ: Lower Limit Of Quantification

VYN201: Phase 1a SAD/MAD Study (Complete)

Positive safety results support thesis for developing VYN201 as locally-administered, soft drug to maximize target engagement and minimize system exposure

Study Design

A single ascending / multiple ascending dose cohort in healthy volunteer participants for up to 2 weeks of once-daily treatment

- N=30: 5 Cohorts with 6 patients each, evaluating 0.025%, 0.1%, 0.5%, 1.0% and 2.0% strengths
- Assessments included TEAEs, pharmacokinetics and local skin tolerance

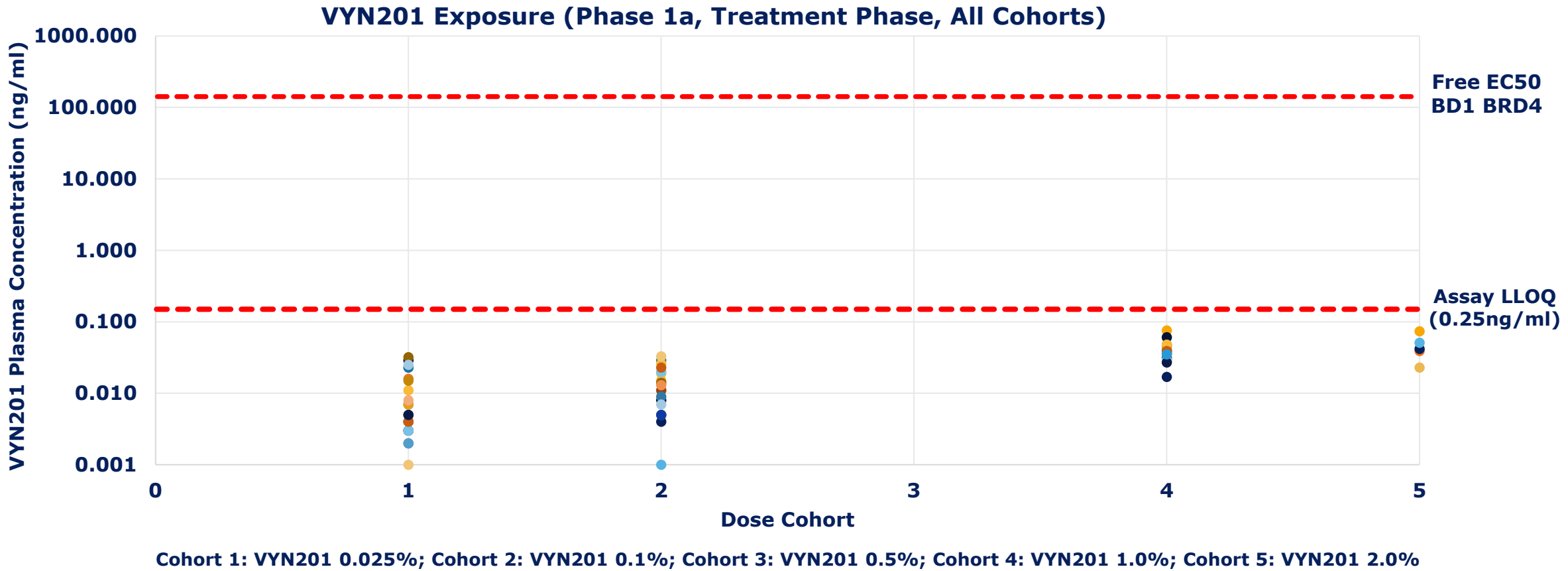
Summary of Results

- **VYN201 was generally well-tolerated with no clinically relevant TEAEs, meeting the primary objective of the study**
  - No SAEs and no dose adjustments were required; No clinically relevant treatment emergent adverse events, abnormal clinical laboratory results or electrocardiogram findings
  - No healthy volunteers withdrew from the trial for any reason
- **No quantifiable VYN201 plasma concentrations above the assay LLOQ (0.25 ng/ml) supports "soft" drug approach for topical pan-BD BET inhibitor**
- **All hematological parameters, including platelet counts, were within normal ranges, a finding which has not previously been observed with systemically administered pan-BD BET inhibitor**
- **0.5%, 1.0% and 2.0% strengths selected for evaluation in the Phase 1b study evaluating VYN201 in active vitiligo patients**

TEAE = Treatment Emergent Adverse Events

VYN201 Phase 1a: Clinical Exposure in Healthy Volunteers

No quantifiable VYN201 plasma concentrations above the assay LLOQ supports "soft" drug approach for topical pan-BD BET inhibitor

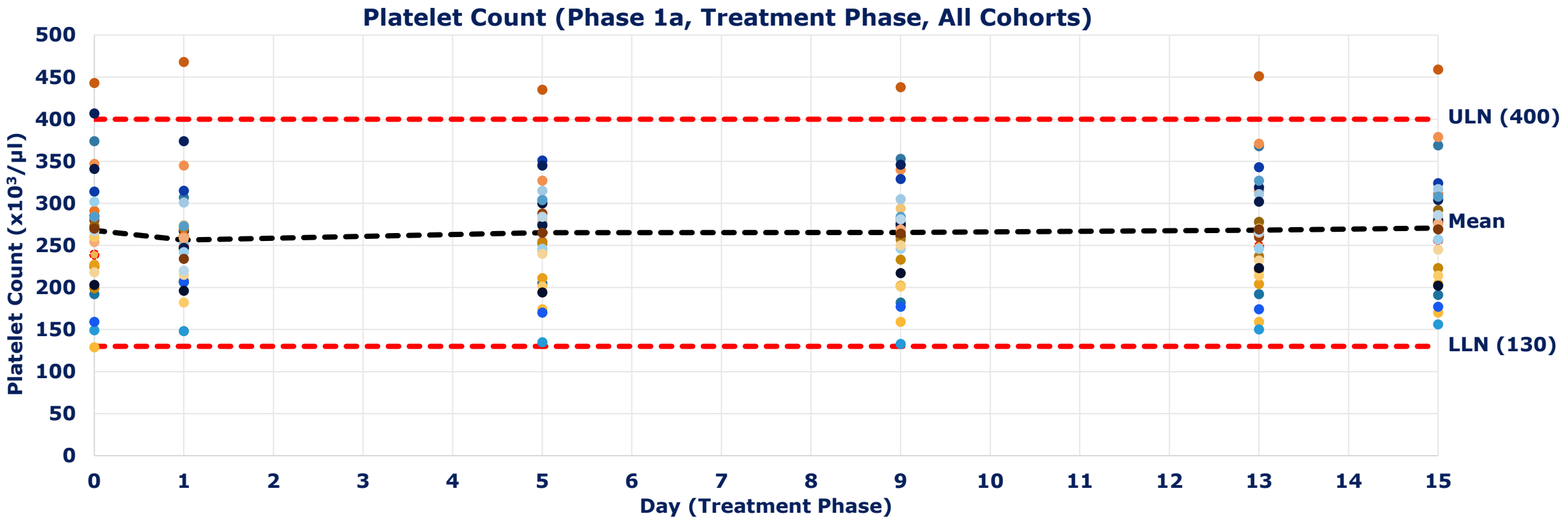


- VYN201 plasma concentrations markedly below free EC50BD1 BRD4 at all dose levels
- All clinical plasma concentrations were below assay lower limit of quantification (LLOQ:0.25ng/ml)
- Assay LLOQ is 720-fold lower than the free $EC50_{BD1\ BRD4}$ for VYN201

LLOQ = Lower Limit of Quantification

VYN201 Phase 1a: Clinical Hematology in Healthy Volunteers

All hematological parameters, including platelet counts, were within normal ranges, a finding which has not previously been observed with systemically administered pan-BD BET inhibitors



- All platelet counts were within normal range
- No trends suggestive of reducing counts by treatment duration or increasing dose
- Similar lack of effect on neutrophils, eosinophils, lymphocytes, basophils and monocytes (data on file)

VYN201: Phase 1b Study in Active Vitiligo Patients

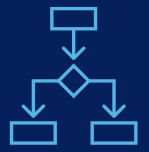
Preliminary P1b safety and efficacy data anticipated in Q3 2023

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 with up to 10 patients each, 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

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

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Vitiligo Disease Activity within POC Study Designs

Patient Population and Asset Development Status

	Disease Activity	Status
VYN201 P1b *(VYNE)*	• Active Only	• Phase 1b is ongoing
Litfulo (Ritlecitinib) P2b[1] *(Pfizer)*	• Active Only	• Pfizer currently enrolling P3 study evaluating 50 mg QD dose in active & passive disease
Povorcitinib P2b[2] *(Incyte)*	• **Active & Stable**	• Incyte preparing for Phase 3 program
Opzelura (Ruxolitinib) P2b[3] *(Incyte)*	• **Active & Stable**	• 1.5% BID dose approved in the U.S. (July 2022) and EU (April 2023)
Rinvoq (Upadacitinib) P2b[4] *(AbbVie)*	• **Active & Stable**	• Phase 2b is ongoing

If P1b study is successful, VYNE expects to enroll patients with active and stable disease in future trials

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

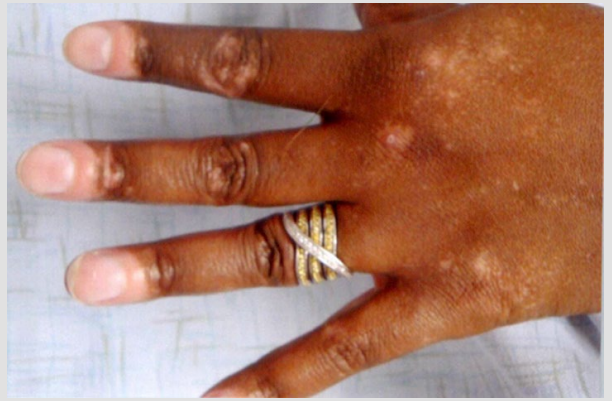
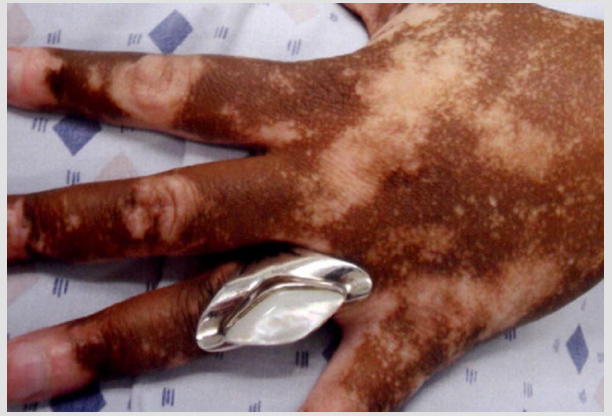


Fig 2:
16 weeks later Showing extension of depigmentation and new areas of confetti-like depigmentation



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

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

Vitiligo Represents an Exciting Opportunity for VYN201

Positive Phase 1a SAD/MAD study results announced
Preliminary P1b safety and efficacy data anticipated in Q3 2023

Novel Mechanism of Action with Encouraging Data

- VYN201 utilizes a “soft” drug approach designed to maximize target engagement in the skin and minimize systemic exposure
- VYN201 shown to impact key biomarkers and genes that drive dyspigmentation in vitiligo in validated preclinical human tissue model (TNF-α and IFN-ɣ, MMP9 and E-cadherin)
- Preclinical data suggest that VYN201 regulates WNT pathway which is believed to play a key role in melanocyte regeneration
- Favorable P1a SAD/MAD safety and tolerability data

Significant Unmet Need

- Vitiligo is a disabling disease impacting social, sexual and professional life
- Current treatment dominated by non-specific therapeutics
- Only one FDA-approved Rx drug (JAK) which includes a black box warning

Large Market

- 0.5 to 2.0% of worldwide population
- Non-segmental sub-type represents ~90% of patients
- Est. U.S. prevalence is between 1.9 and 3.2 million cases (diagnosed/undiagnosed)

Recent acquisition of Villaris for preclinical vitiligo asset auremolimab underscores the attractive opportunity for VYN201 ($70M upfront / $1.4B total deal value)

Sources: Bergqvist. Dermatol. 2020;236:571-592; *JAMA Dermatology*, “Prevalence of Vitiligo Among Adults in the United States”; 2022; 158(1):43-50 (published online Nov. 17, 2021); Rangu S, McKenzie PL, Castelo-Soccio L (2021) Therapy Utilization among Children with Vitiligo at an Urban Tertiary Care Center J Clin Dermatol Ther 7: 070.

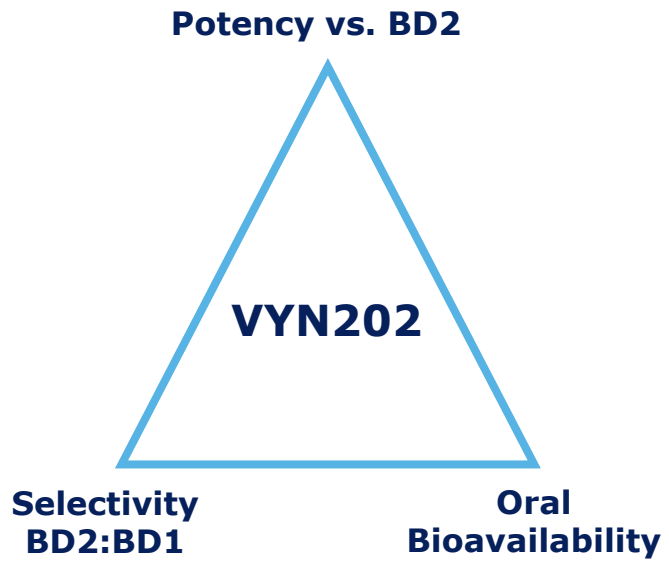
VYN202: BD2 selective BET inhibitor

VYNE™ THERAPEUTICS

VYN202 – Oral BD2-selective BET inhibitor

Designed with class-leading selectivity (BD2 vs. BD1), targeting improved efficacy and tolerability as compared to other systemic pan-BD BET inhibitors in development

Molecular Profile Design



Potential Target Market[1]:

- I&I indications such as RA, psoriasis, systemic lupus erythematosus, UC/Crohn's and multiple sclerosis; additional potential in myeloproliferative neoplastic disorders

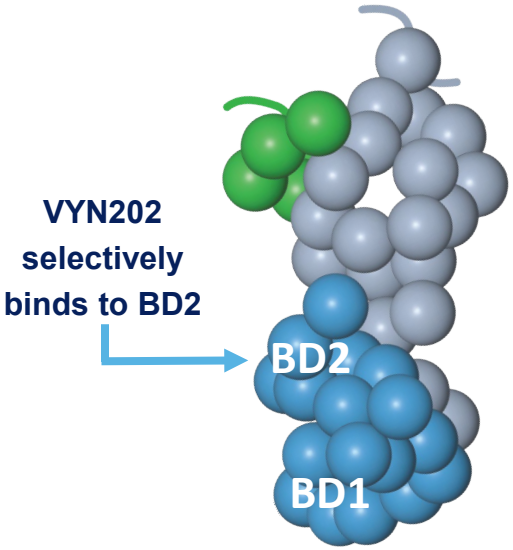
Class Leading Selectivity:

- Potential to be most potent and BD2-selective BET inhibitor in development
- Targeting improved safety profile compared to oral pan-BD BET inhibitors

Targeted Near Term Milestones:

- Q4 2023: Indication Selection; Submit IND

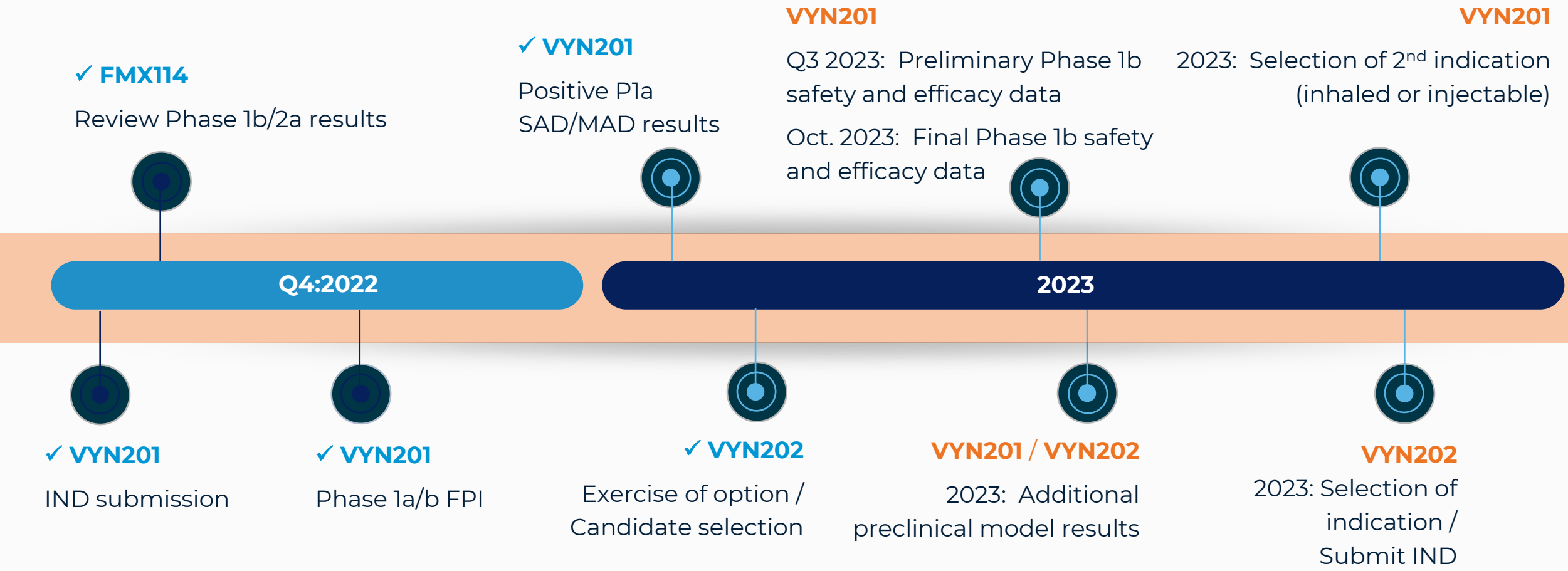
BET Protein



1. Initial indication to be communicated following completion of requisite pre-clinical evaluations. List included is not exhaustive of potential indications

Potential Near-term Value-Creating Milestones

Building a leading early-stage immuno-inflammatory pipeline



Note: Cash runway guidance through the end of 2023 assumes development activities for VYN201 in nonsegmental vitiligo and continued advancement of VYN202, based on current estimates. Refer to slide 2 "Forward Looking Statements" for description of risks and uncertainties regarding the future expectations, plans and prospects of VYNE. Subject to adequate levels of funding.

Appendix: VYN201

VYNE™ THERAPEUTICS

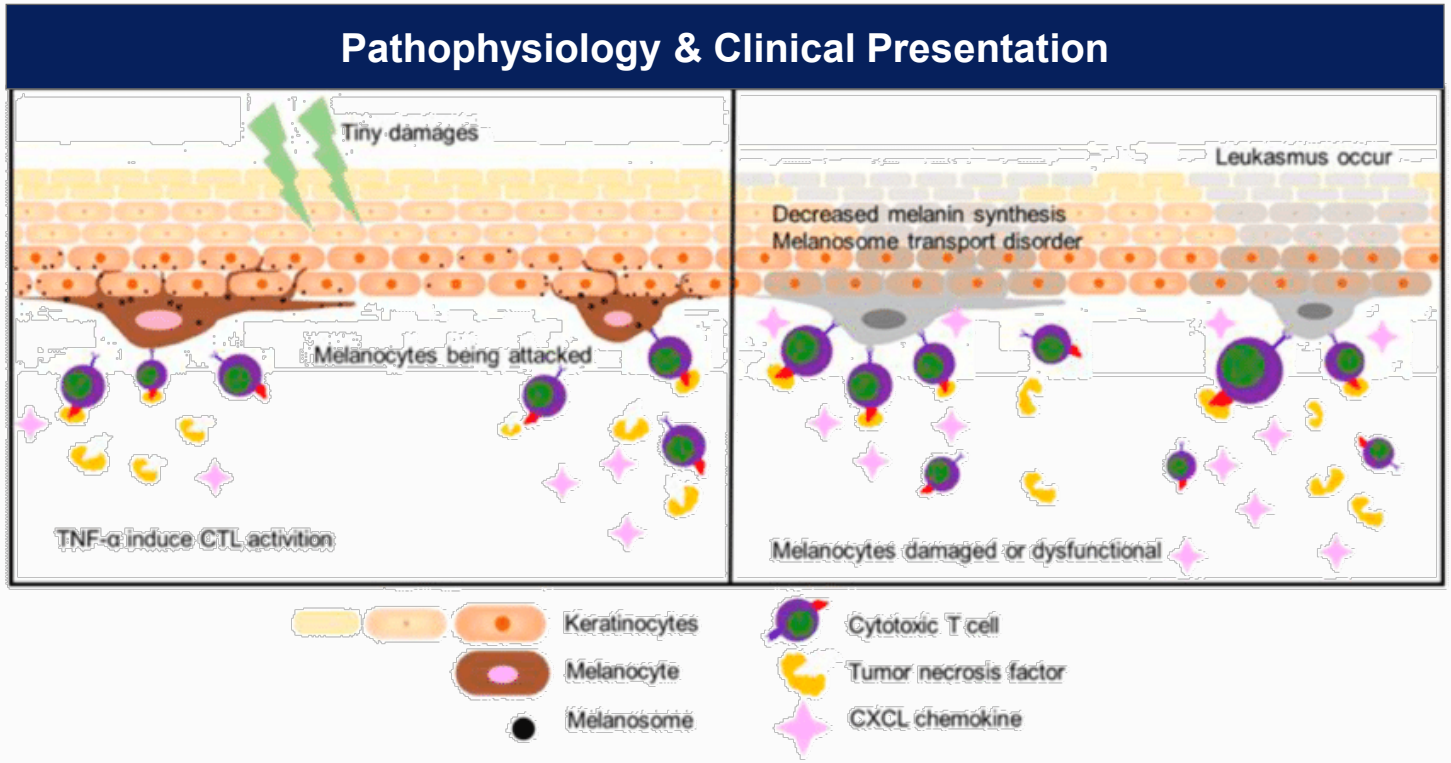
ROOTED IN INNOVATION

VYN201: Vitiligo
Disease / Market Overview

VYNE™ THERAPEUTICS

Vitiligo – Disease Overview

An acquired disorder of dermatologic pigmentation with high impact on self-esteem



- Vitiligo is a depigmenting skin disorder characterized by the **loss of melanocytes,** which causes typical non-scaly, chalky-white macules
- Pathogenesis is classified as **autoimmune in nature**; the disease is associated with a culmination of genetic and environmental factors with metabolic, oxidative stress, and cell detachment abnormalities
- Vitiligo can be classified as segmental or non-segmental; segmental presentation appears **unilaterally**, while non-segmental presents **bilaterally and occasionally mucosally** (i.e., around the mouth)
- Characteristic amelanotic lesions, while physically harmless, **tend to be psychologically devastating**

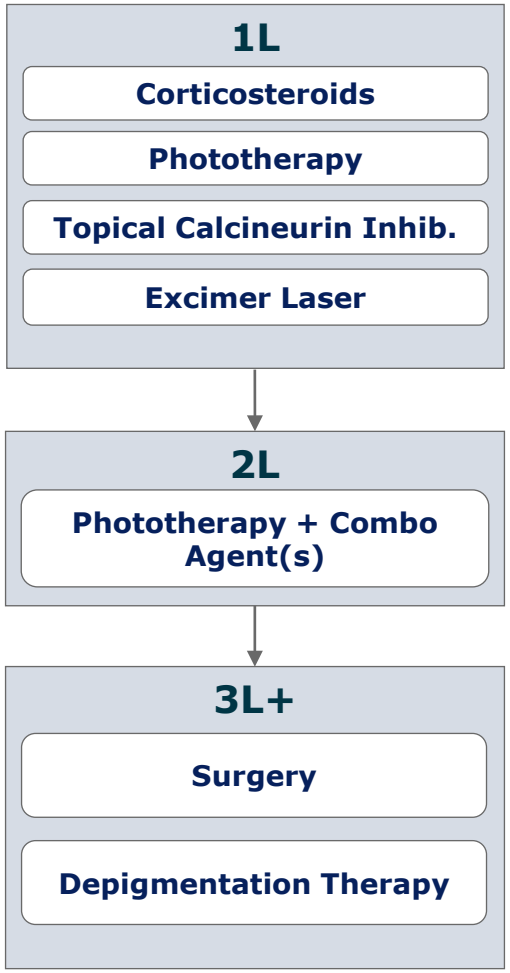
Source: UptoDate; Bergqvist. Dermatol. 2020;236:571-592; Karagaiah. Expert Opin Emerg Drugs. 2020;25(1):7-24

VYNE™ THERAPEUTICS

Vitiligo – Treatment Paradigm

Only one drug currently approved; Treatment is dominated by non-specific therapeutics

Current Treatment Paradigm



Treatment modality is dependent on **disease area** (segmental vs. non-segmental) as well as **activity** (controlled vs. uncontrolled); patients typically receive **NBUVB phototherapy, excimer laser procedure,** or an **oral / topical anti-inflammatory agent in the 1L**

1L agents are often **used in combination in the 2L** to enhance disease control

Surgeries include skin tissue / cellular grafting and hair follicle transplant, often **technically challenging and costly**; depigmentation therapy is a **less common FDA-approved modality for cosmetic improvement**

Vitiligo Key Unmet Need

Current vitiligo treatment is dominated by non-specific therapeutics with only one drug recently approved with a black box warning

A **targeted, safe and more efficacious treatment option is needed** that lowers the disease recurrence rate and is effective for all skin tones / scar types

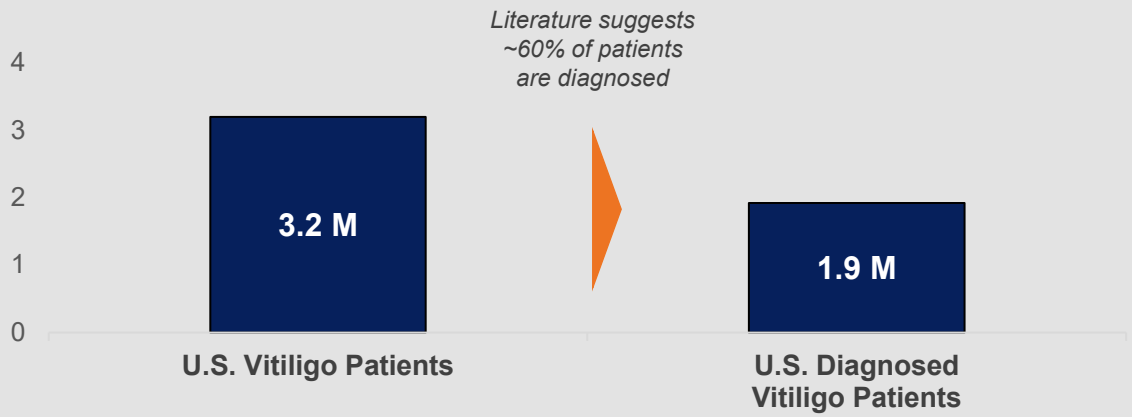
Source: UptoDate; Bergqvist. Dermatol. 2020;236:571-592; Karagaiah. Expert Opin Emerg Drugs. 2020;25(1):7-24
NBUVB: Narrow-band ultraviolet-B light

VYNE™ THERAPEUTICS

Vitiligo – Epidemiology and Pricing

Large market with high unmet need and lack of approved prescription treatment options

U.S. Addressable Patients



- **Large U.S. market U.S. Patients with Vitiligo: ~3.2 M with only 1 approved Rx drug treatment**
  - Prevalence generally consistent across regions of the world with a range of 0.5% to 2.0% of the worldwide population
- **Prevalent U.S. Patients with Diagnosed Vitiligo: ~1.9 M**
  - ~60% of prevalent vitiligo in the U.S. is clinically-diagnosed
  - Literature suggests that many patients do not currently seek treatment due to lack of approved and effective treatment options

U.S. Pricing Potential / Analogs

- A topical product as an alternative to steroids and/or calcineurin inhibitors or a JAK with black box warning would be well-received in a market with limited approved therapies;
- Anticipate payer and market access landscape to be favorable
- A relevant price comparator for a novel treatment of vitiligo may be newly FDA-approved Opzelura™ (ruxolitinib), **a topical JAK inhibitor with a black box warning, targeting AD and vitiligo (July 2022)**
- Opzelura™ is priced at ~$2 K per 60g tube or $20 K annually assuming guidance ~10 tubes on average per year for vitiligo

Current Annual Opzelura Price Expectation:

~$20 K

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; Incyte Corporate Pres.; Redbook; Rxlist.com MOA: Mechanism of action; sNDA: Supplemental new drug application.[1] Data also suggest a small percentage of pediatrics (i.e., 0.24%) affected by vitiligo; Vitiligo prevalence is fairly-consistent across different regions according to Kruger (2012)

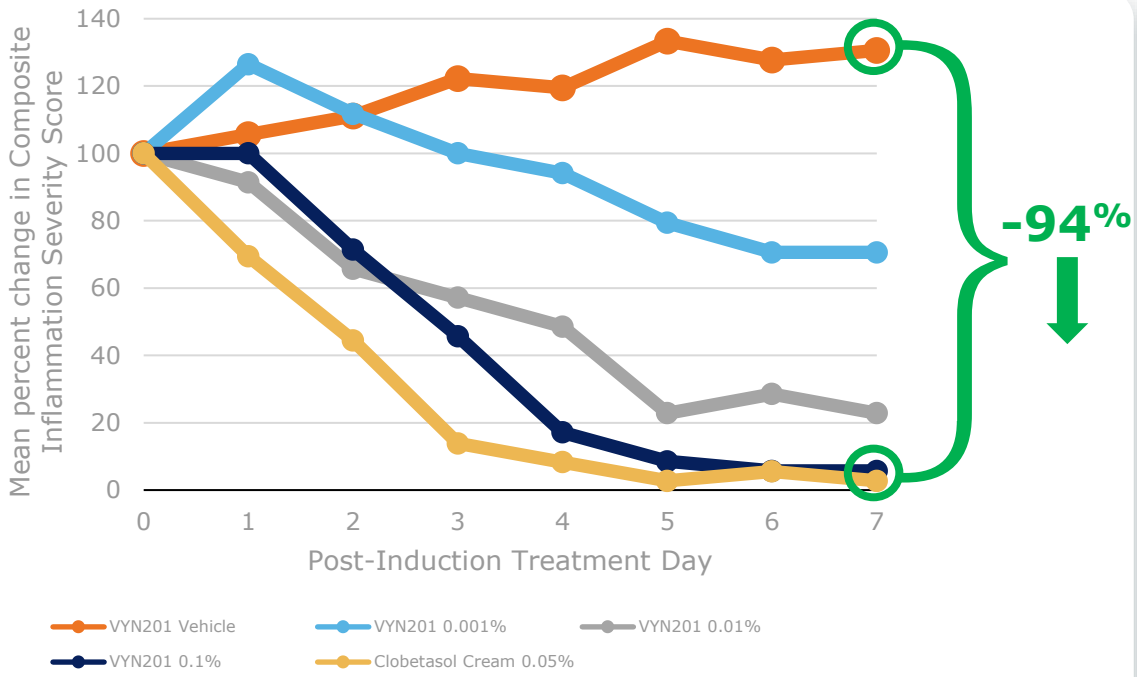
VYNE™ THERAPEUTICS

VYN201: Th17 Inflammation Model

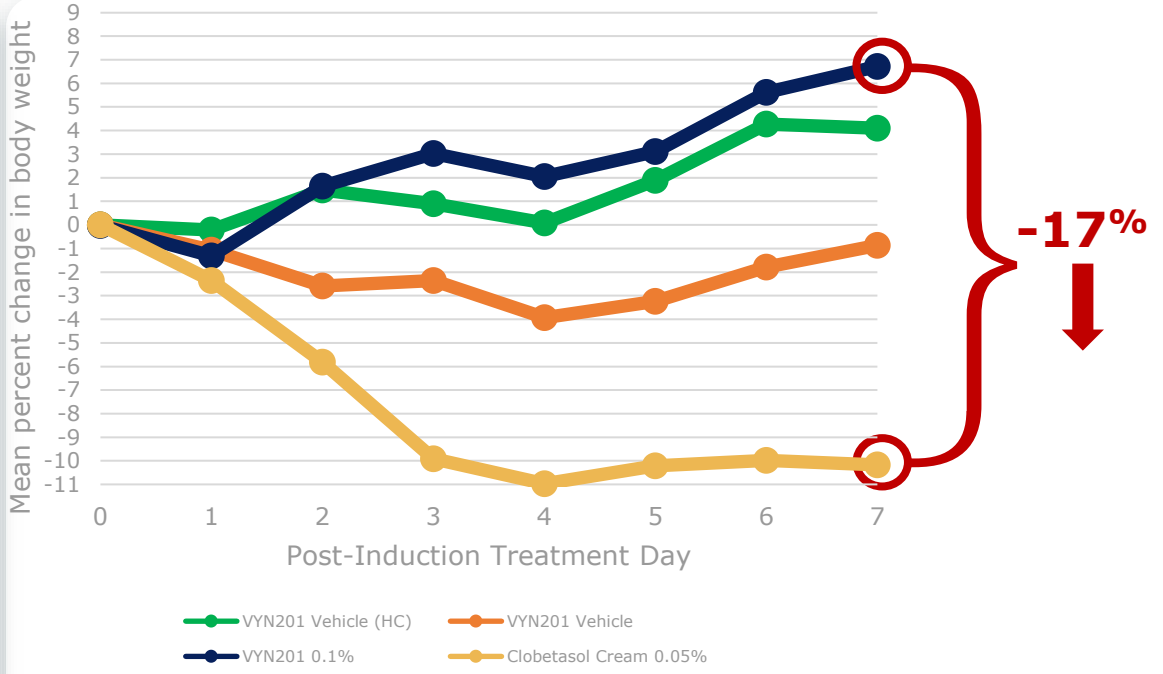
VYNE™ THERAPEUTICS

VYN201: Comparable Efficacy to Superpotent Steroid Clobetasol
in a TH17-Mediated Murine Inflammation Model; Potential for Greater Tolerability

Dorsal depilated BALB-C mice were dosed topically for 14 days with 100mg topical IMI cream (Day 1-7: induction phase, Day 8-14: treatment phase). N=4 animals were assigned to each treatment group with each group receiving 100mg of allocated treatment on Day 8-14 once daily



- Dose dependent response was observed over the VYN201 concentration range 0.001% to 0.1%
- There was a 94% reduction in composite score for VYN201 0.1% relative to vehicle control group at Day 7
- VYN201 0.1% had comparable efficacy to clobetasol propionate 0.05% cream



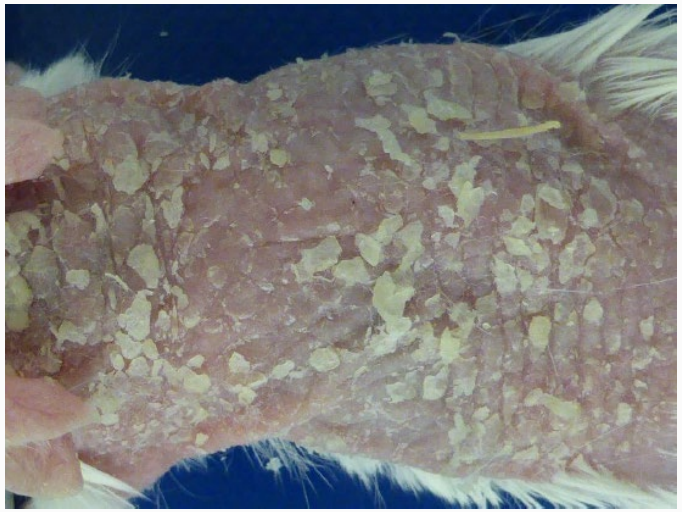
- Animals treated with VYN201 0.1% continued to gain body weight in a similar manner to healthy control group treated with vehicle
- Clobetasol cream 0.05% group had a 17% reduction in body weight compared to the VYN201 0.1% group at treatment day 7

IMI – Imiquimod.

*Composite Inflammation Severity Score is a composite mean score of erythema and peeling severity scored on a 4-point ordinal scale per domain (0=none, 1=mild, 2=moderate and 3=severe for a maximum score of 6), data expressed as a mean percentage change from initiation of treatment phase.

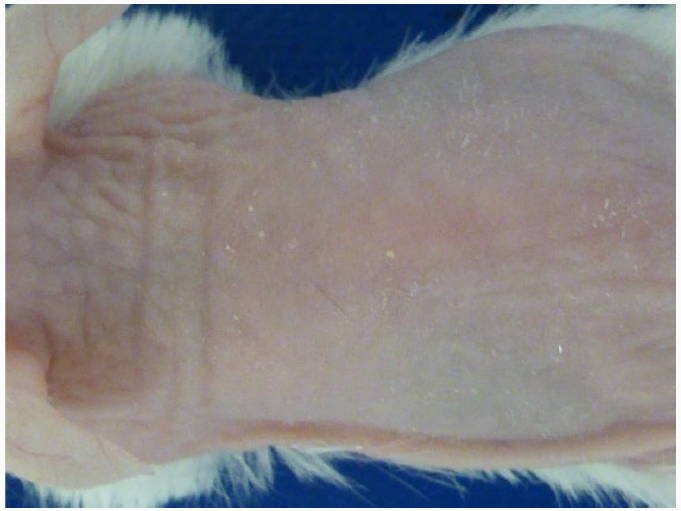
VYNE™ THERAPEUTICS

VYN201:
Normal Skin Physiology in TH17-Mediated Murine Inflammation Model Suggests VYN201 Well Tolerated (Day 7)



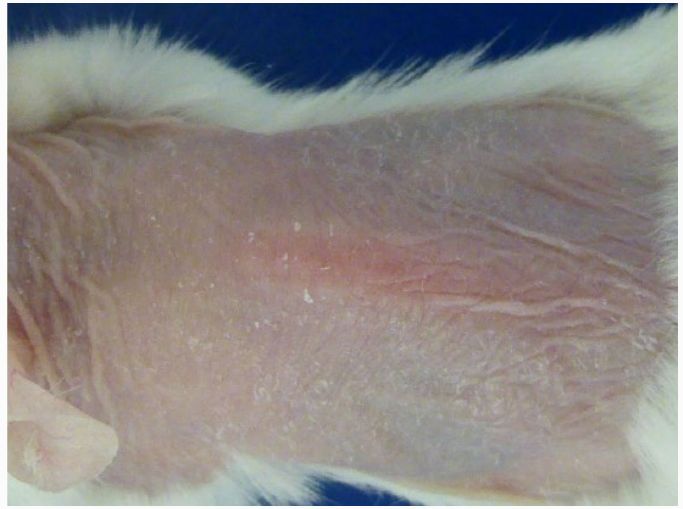
VYN201 Vehicle

- No appreciable improvement in clinical signs



VYN201 0.1%

- Substantial resolution of clinical signs
- Skin presents with normal physiology with no evidence of striae rubrae or atrophy
- No evidence suggestive of intolerance

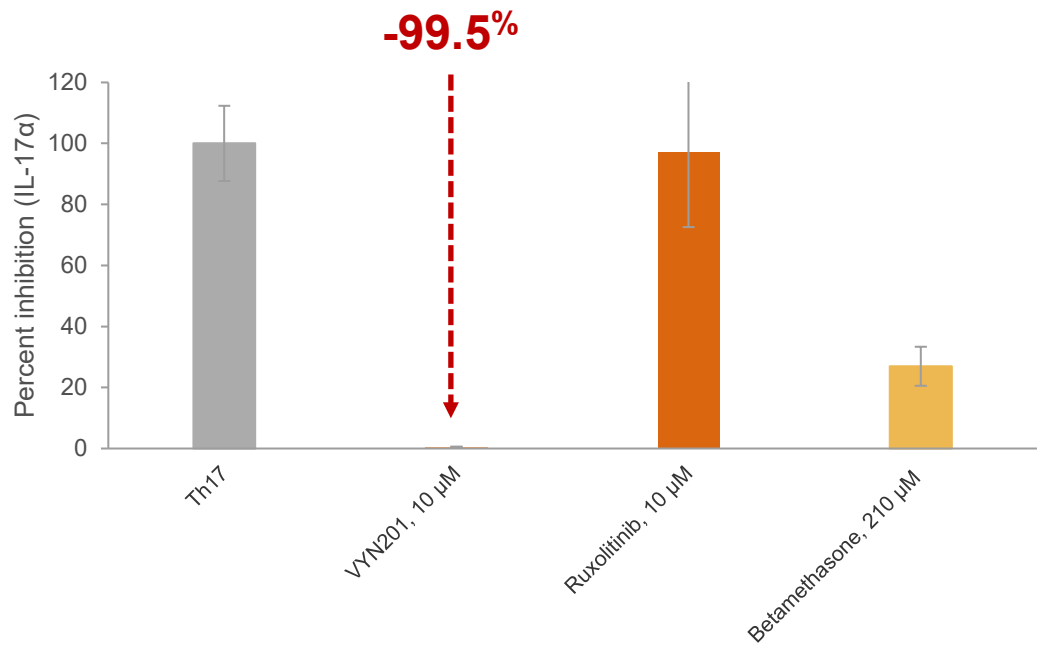


Clobetasol Cream 0.05%

- Substantial resolution of clinical signs
- Significant evidence of dermal atrophy (clear presence of both rhytides/fine wrinkles and deep wrinkles)
- Marked dermal translucency and elastolysis

VYNE™ THERAPEUTICS

VYN201 Significantly Reduced Expression of Several Key Pro-Inflammatory Proteins Relevant to Th17-mediated Autoimmune Diseases in Human Tissue[1]



Interleukin 17-alpha

T-cells are polarized to Th1 and Th17 cells, the latter of which drives the production of IL17a which further upregulates the migratory action of pro-inflammatory cells and further inflammatory cell activation.

>95% Inhibition seen with assays for IL-36γ & LP-10

Interleukin 36-gamma

IL36γ is implicated in upregulating IL-17A signaling-related genes and so able to amplify keratinocyte inflammatory responses by promoting not only their own expression but also that of other cytokines related to Th17 signaling

CXC motif chemokine ligand 10 (LP-10)

An inflammatory cell chemoattractant secreted in response to interferon gamma. LP-10 is significantly overexpressed in many autoimmune diseases (>25-fold) vs. healthy skin[1]

1. Data on file. Results presented from qPCR analysis of processed and Th17-stimulated ex vivo human skin tissue based on a method derived from Garrett S.M., Zhao Q., and Feghali-Bostwick C. (2019) Induction of a Th17 phenotype in human skin – a mimic of dermal inflammatory diseases, *Methods and Protocols*, 2, 45

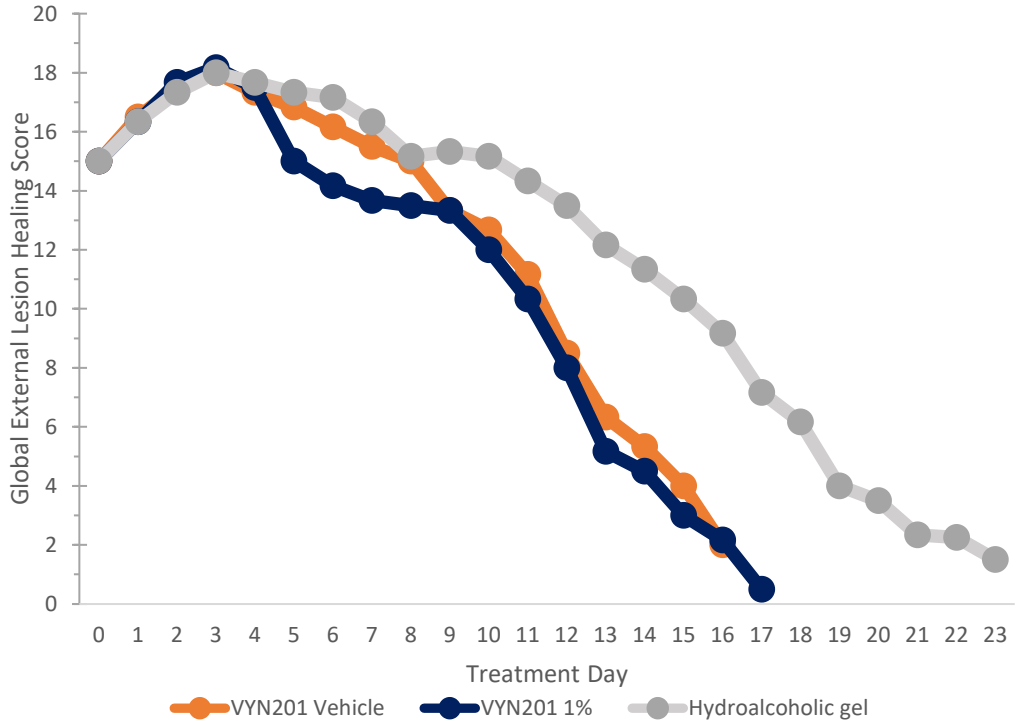
VYNE™ THERAPEUTICS

VYN201: Fibrotic Tissue & IPF Models

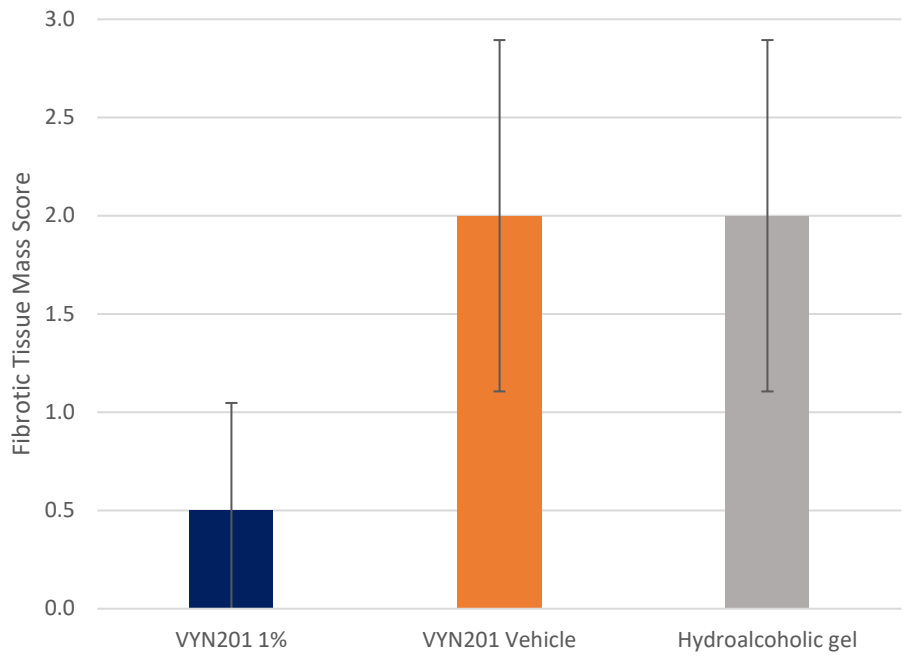
VYNE™ THERAPEUTICS

VYN201: Demonstrated Anti-Fibrotic Activity
without Delay in Healing Time in Murine Skin Healing Model

Female hairless mice (n=4/group) had two identical 10mm incisions made either side of the flank. Animals were topically dosed 1X daily with 100mg VYN201 vehicle, VYN201 1% or a Hydroalcoholic gel* until each wound had completely healed



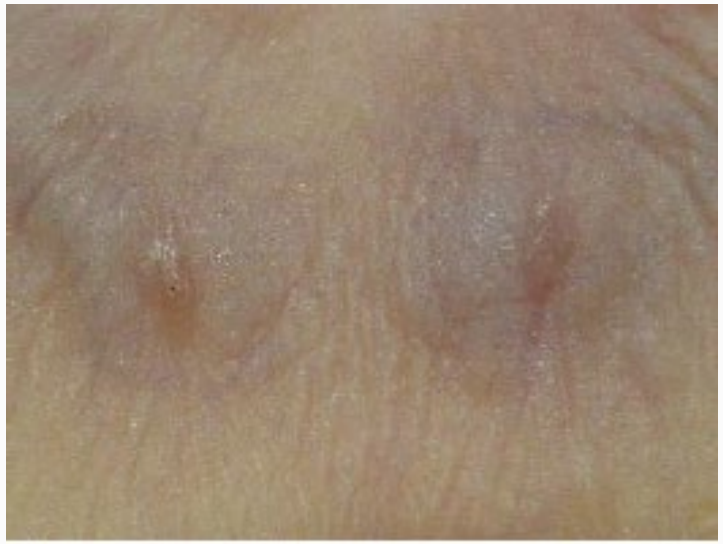
- Statistically significant difference ($p<0.05$) in composite global external healing score for VYN201 1% compared to Hydroalcoholic gel from Day 8
- Complete healing occurred for VYN201 1% and VYN201 vehicle approximately 5 days earlier compared to Hydroalcoholic gel (Mean day to heal:15.5 vs. 21 days)



- Animals treated with VYN201 1% had statistically significant less tissue mass/fibrosis compared to VYN201 vehicle or Hydroalcoholic gel, indicative of the known anti-fibrotic mechanism for BET inhibition ($P<0.05$ for VYN201 1% compared to VYN201 vehicle and Hydroalcoholic gel)

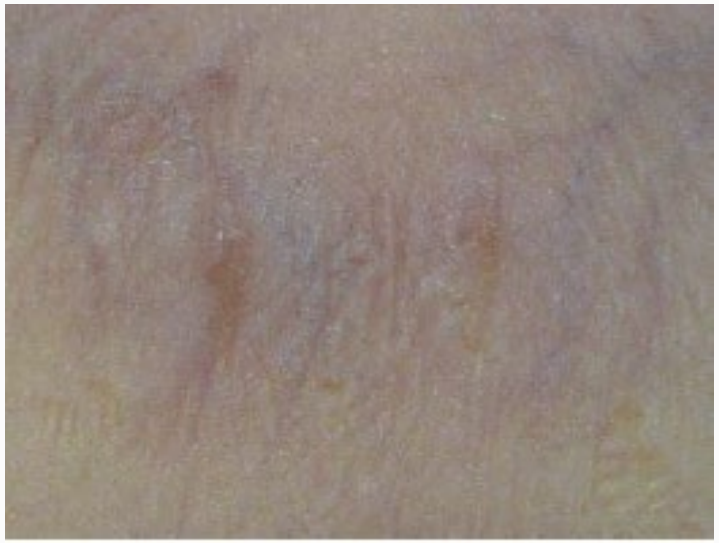
*A negative control known to delay wound healing
Global External Lesion Score is a composite severity score of lesion length, width, swelling and visibility
Fibrotic tissue mass is scored on a 4-point severity scale: 0=No tissue mass; 1=small tissue mass; 2=moderate tissue mass; 3=large tissue mass

VYN201: Little Evidence of Residual Swelling
and Macular Wound Appearance in Murine Skin Healing Model



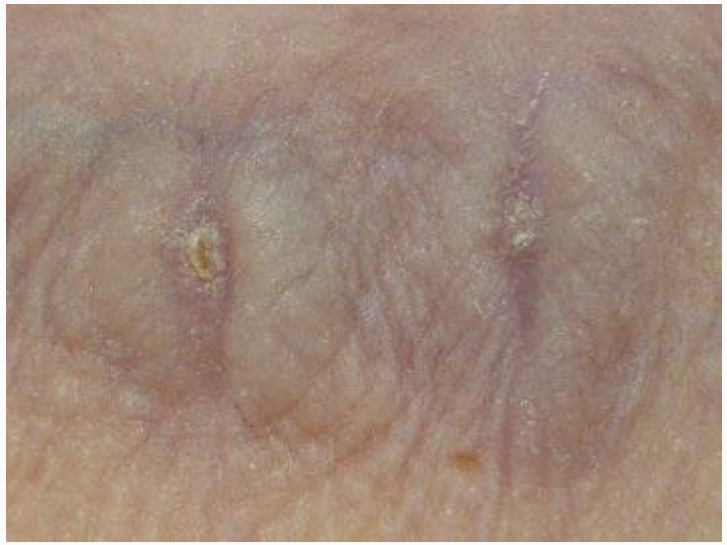
VYN201 Vehicle

- Still evidence of minor swelling around incision sites



VYN201 1%

- Little evidence of residual swelling
- Wound appears more macular in nature compared to VYN201 vehicle or the Hydroalcoholic gel
- Incision sites appear less distinct and leave a more aesthetic outcome compared to other treatments

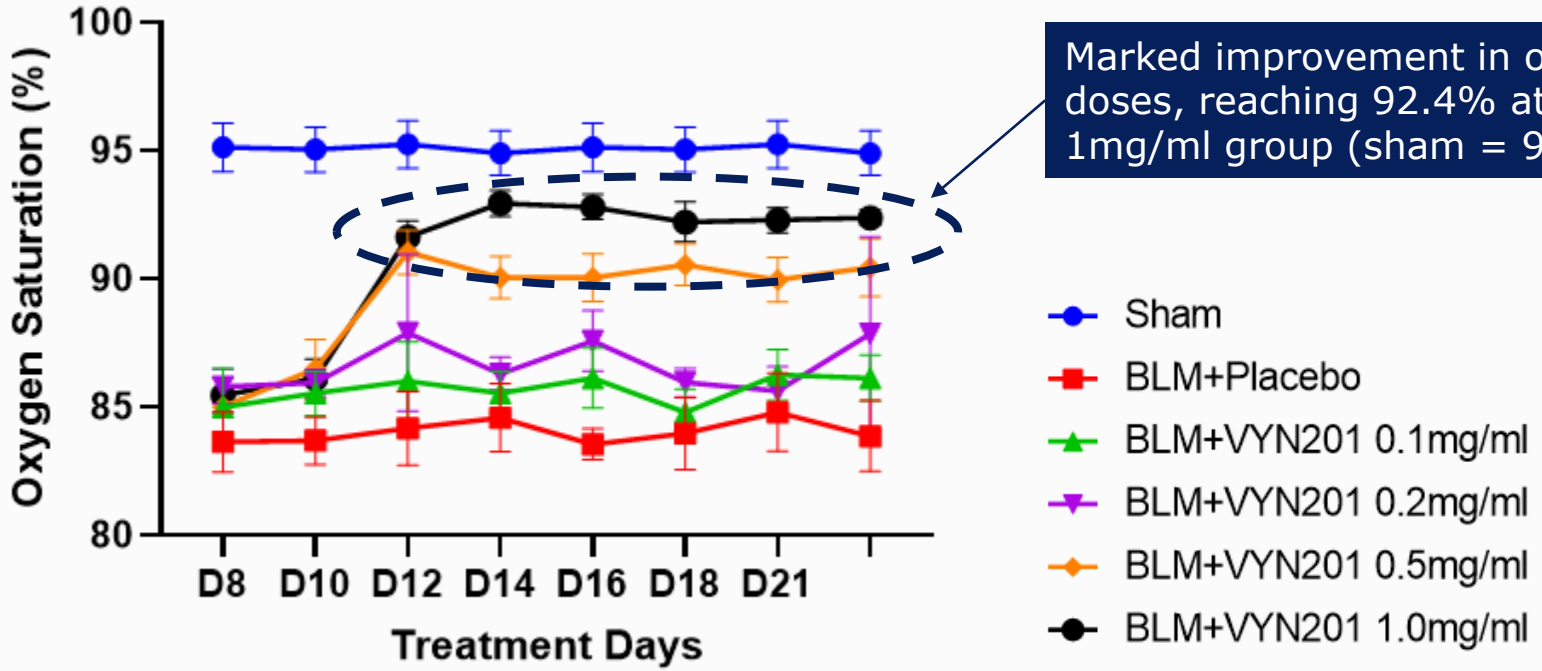


Hydroalcoholic gel

- Moderate swelling clearly evident at end of treatment
- Although healed, residual scabbing still remains
- Incision sites clearly visible

VYN201: Bleomycin-Induced Mouse Model of Pulmonary Fibrosis

Marked improvement in oxygen saturation after three doses



Marked improvement in oxygen saturation after just 3 doses, reaching 92.4% at Day 21 for the VYN201 1mg/ml group (sham = 95.2% at Day 21)

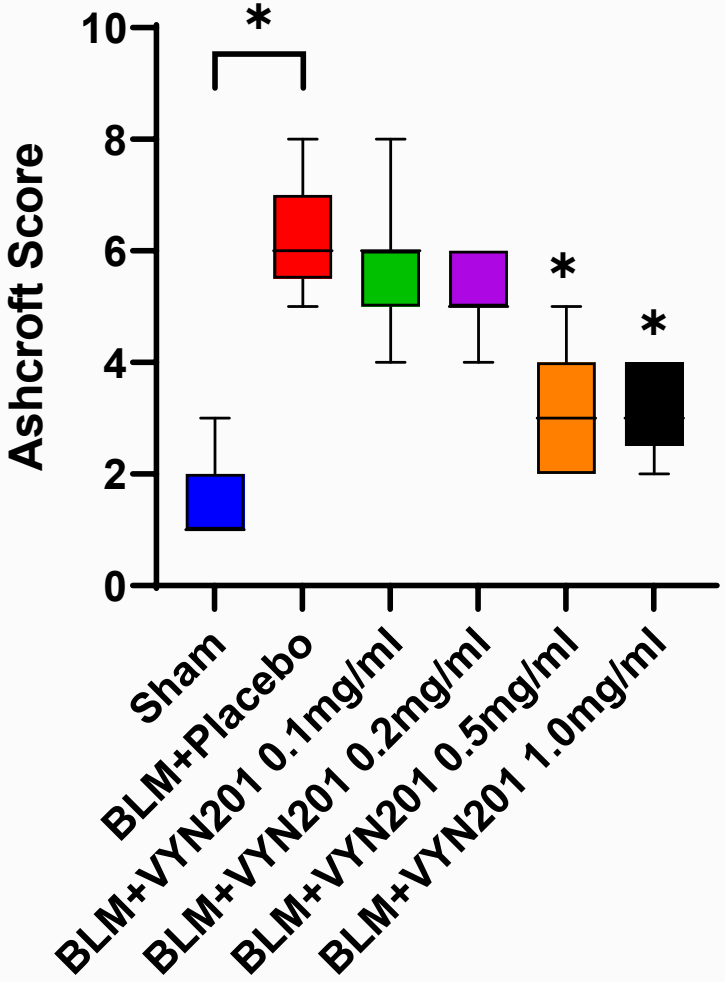
- VYN201 demonstrated a dose-dependent improvement in blood oxygen saturation over the dose range 0.1 to 1mg/ml
- Mean blood oxygen saturation for the VYN201 1mg/ml group was 92.4% at Day 21, an 8.8% improvement compared to the placebo group (83.6%)
- Mean blood oxygen saturation for the sham (unstimulated and untreated) control group was 95.2%

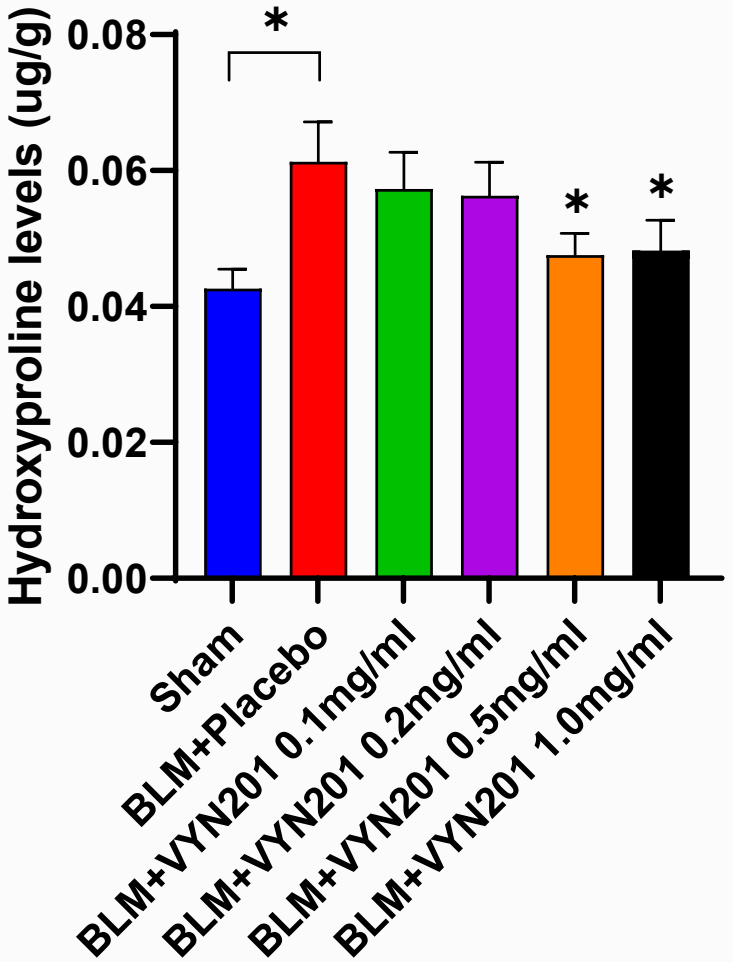
Lung fibrosis was induced in 12-week-old C57Bl/6 male mice using a single dose of 1U/kg bleomycin, dosed IT. Fibrosis was left to develop over 7 days and thoracic tomography images were obtained to stage fibrotic development. Animals were assigned to six treatment groups (Not treated control, vehicle, and VYN201 at 0.1, 0.2, 0.5, and 1.0mg/ml [N=6/group]). Each treatment group was dosed QOD OP for a further 14 days. Change in body weight, volumetric lung function, blood O_2 saturation, lung hydroxyproline and Ashcroft fibrotic scoring were assessed.

VYNE™ THERAPEUTICS

VYN201: Bleomycin-Induced Mouse Model of Pulmonary Fibrosis

Significant reductions in both lung fibrosis and hydroxyproline[1]





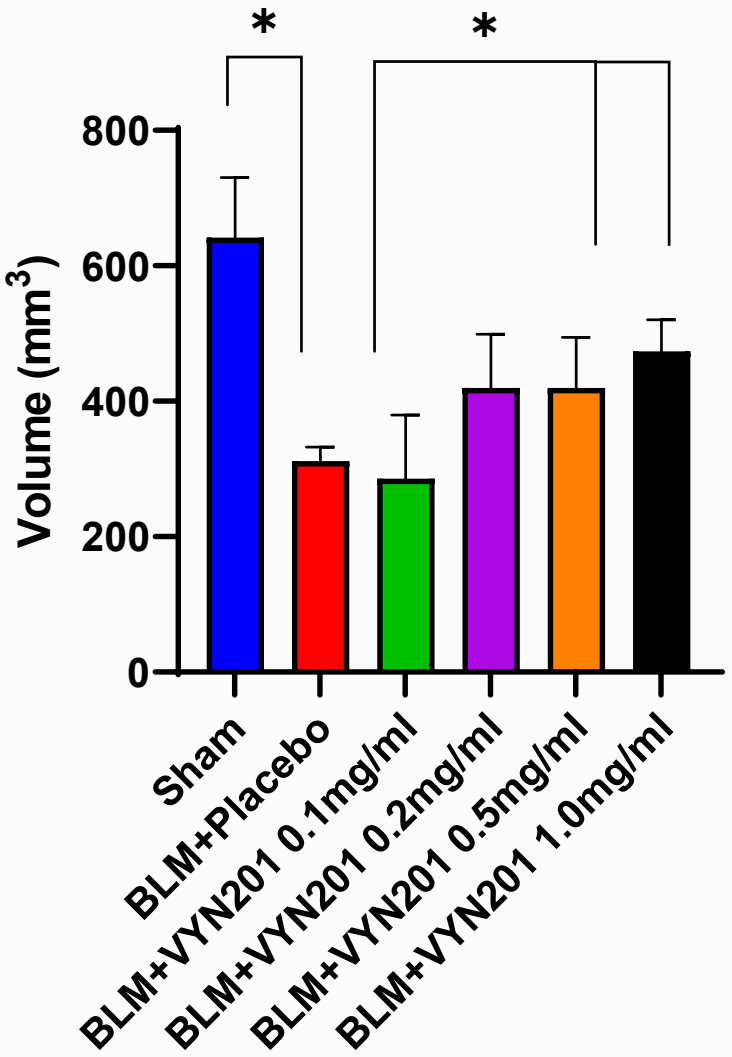
- VYN201 at 0.5mg/ml and 1mg/ml demonstrated statistically significant reductions in Ashcroft scores (a measurement of lung fibrosis) and levels of the tissue fibrosis biomarker, hydroxyproline, compared to placebo at Day 21
- Mean control-adjusted lung fibrosis scores for VYN201 1mg/ml were 65.8% lower compared to the placebo control group at Day 21

Sham=Not treated
*=p<0.05, Mann-Whitney test
1. Hydroxyproline is a tissue biomarker for fibrosis

VYNE™ THERAPEUTICS

VYN201: Bleomycin-Induced Mouse Model of Pulmonary Fibrosis

>50% increase in functional lung volume compared to placebo



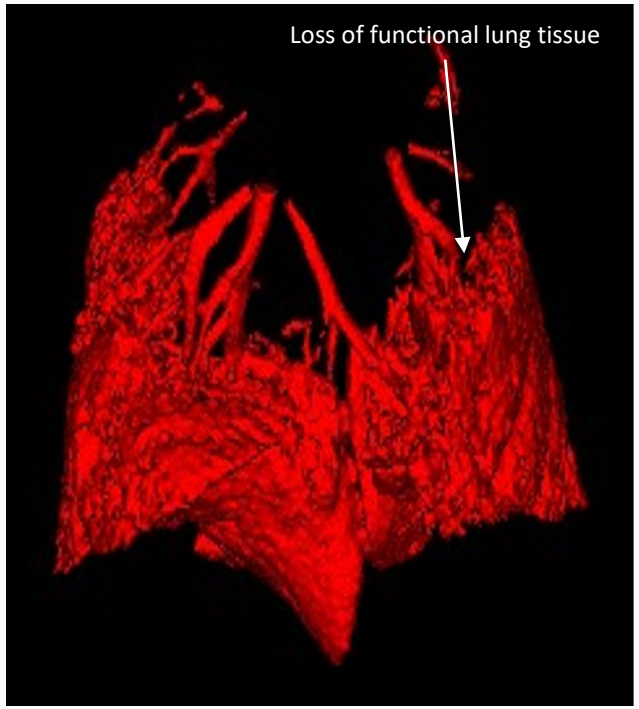
- Dose dependent improvement in functional lung volume for groups treated with VYN201
  - Correlates with an increase in blood oxygen saturation and reduction in Ashcroft fibrosis scores
- VYN201 1mg/ml demonstrated a 51.8% mean improvement in functional lung volume compared to animals receiving placebo treatment

*=p<0.05, Mann-Whitney test

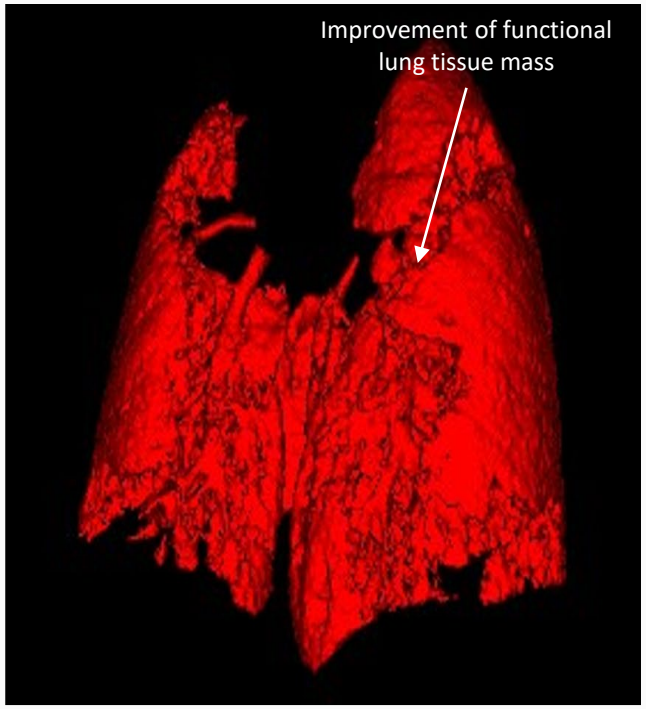
VYN201: Bleomycin-Induced Mouse Model of Pulmonary Fibrosis

Representative CT images showing detectible loss in functional lung volume

Sham (Untreated/un-stimulated)



Bleomycin + Placebo



Bleomycin + VYN201 1mg/ml

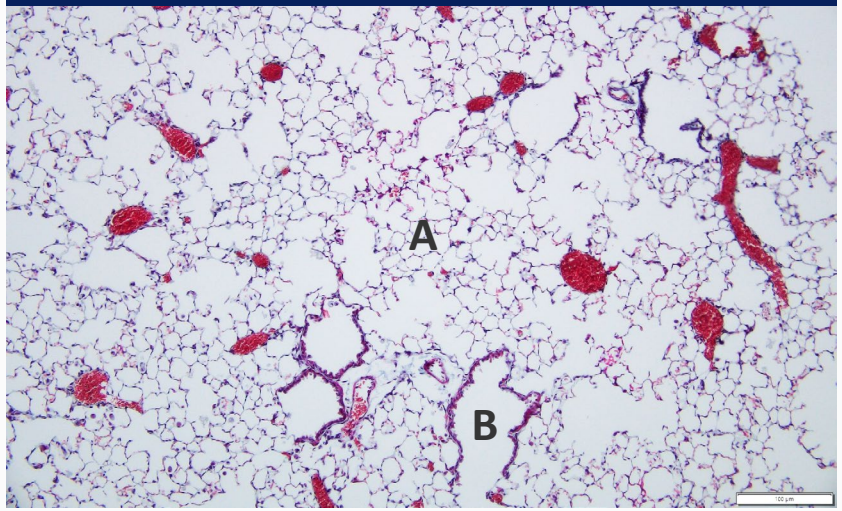
- VYN201 demonstrated a marked, dose-dependent improvement in functional lung volume compared to placebo
- Functional lung volume improvement correlates with increase in blood oxygen saturation and reduction in Ashcroft fibrosis scores

VYNE™ THERAPEUTICS

VYN201: Bleomycin-Induced Mouse Model of Pulmonary Fibrosis

VYN201 treatment supported significant lung recovery by reducing fibrotic tissue deposition compared to placebo treatment

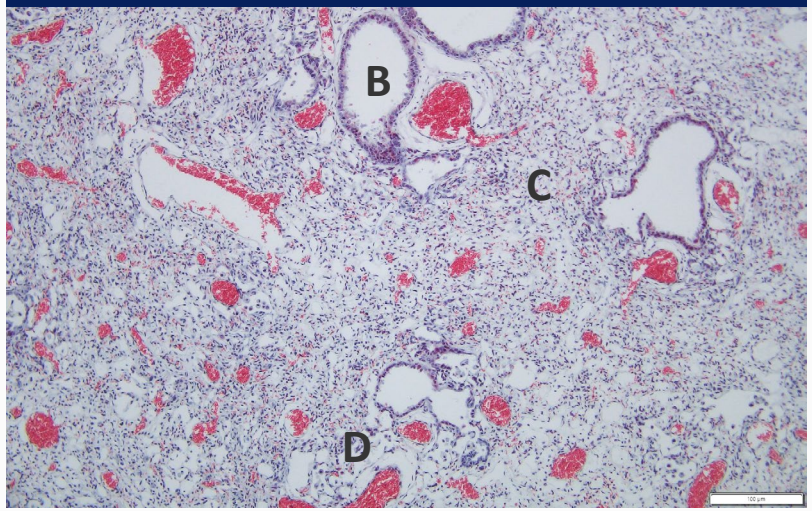
Sham



A: Normal lung parenchyma with open airways and airspaces

B: Conducting airway

Bleomycin + Placebo

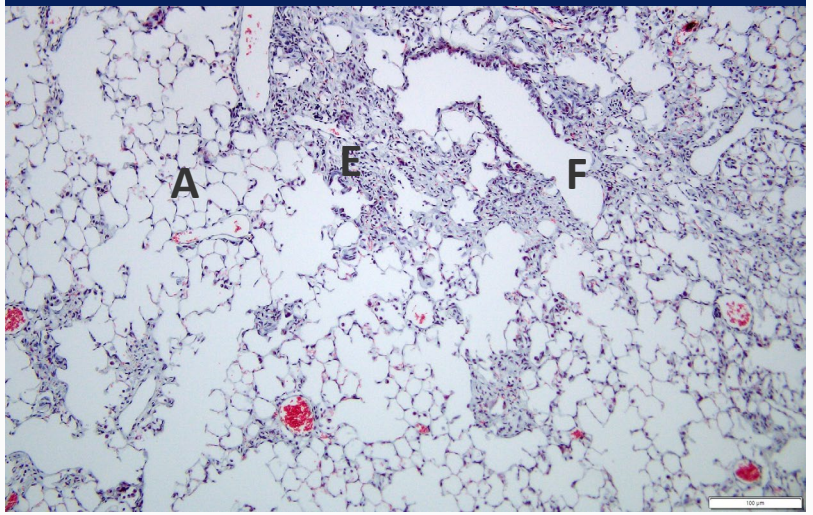


B: Conducting airway

C: Fibrotic lesions with abundant cellularity

D: Sporadic airways

Bleomycin + VYN201 1 mg/ml



A: Normal lung parenchyma with open airways and airspaces

E: Less severe localized fibrosis: parenchyma

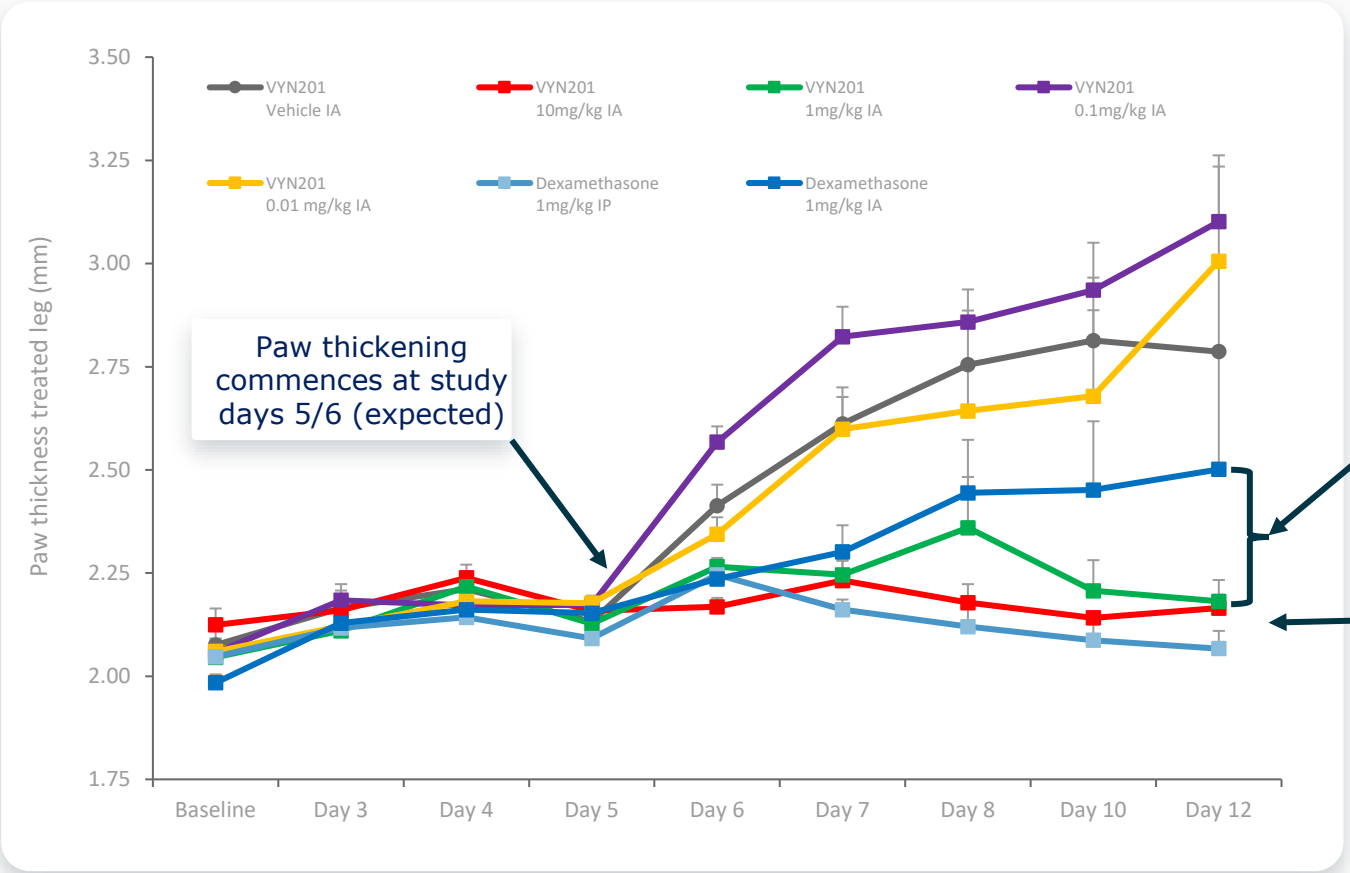
F: Less severe localized fibrosis: airway

VYN201: Arthritis

VYN201: CAIA Mouse Model of Arthritis – Paw Thickness

Marked inhibition of paw thickening/swelling

Inflammatory arthritis was induced in BALB/C mice using a mixture of four arthritogenic MAbs by IV injection at Day 0 and was further challenged with an LPS IV injection at Day 4 (N=7/treatment group). VYN201 treatment groups received 50µl intra-articular (IA) doses of VYN201 at 0, 0.01, 0.1, 1 or 10mg/kg on Days 0, 3, 6 and 9. Dexamethasone control animals received 50µl of 10mg/kg IA on Days 0, 3, 6 and 9 or 1mg/kg intraperitoneal (IP) on each treatment day (Day 0-11). Treatment response was evaluated based on an assessment of paw thickening/swelling.



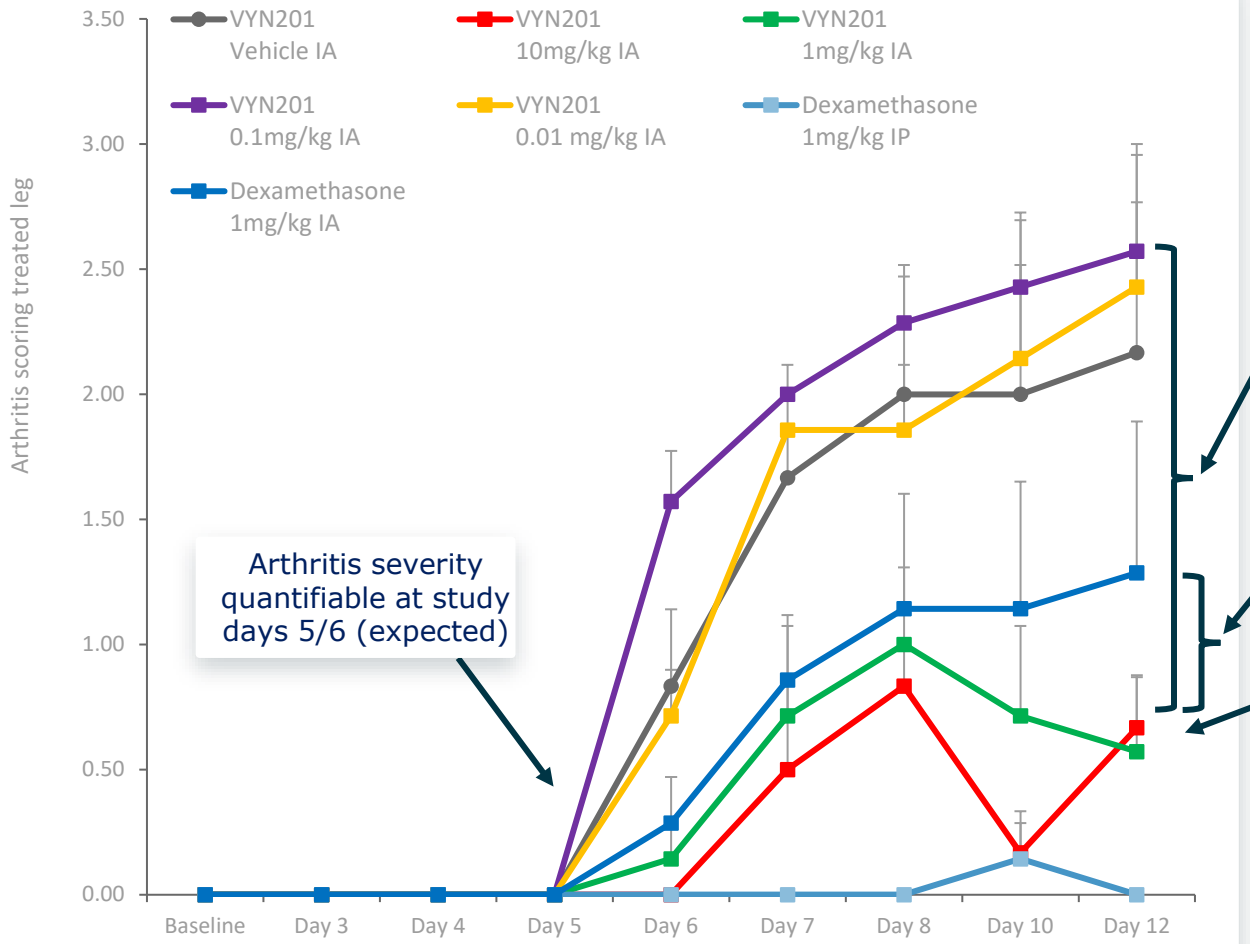
Both VYN201 1 & 10mg/kg superior to dexamethasone IA 10mg/kg

Marked inhibition of paw thickening for the VYN201 1 & 10mg/kg dose levels and in line with 1mg/kg dexamethasone systemic dose

CAIA = Collagen Antibody Induced Arthritis; IA = Intra-articular; IP = Intraperitoneal

VYN201: CAIA Mouse Model of Arthritis – Arthritis Score

Demonstrated dose dependent reduction in disease severity



Clear dose-response demonstrated between VYN201-treated groups

Both VYN201 1 & 10mg/kg superior to dexamethasone IA 10mg/kg

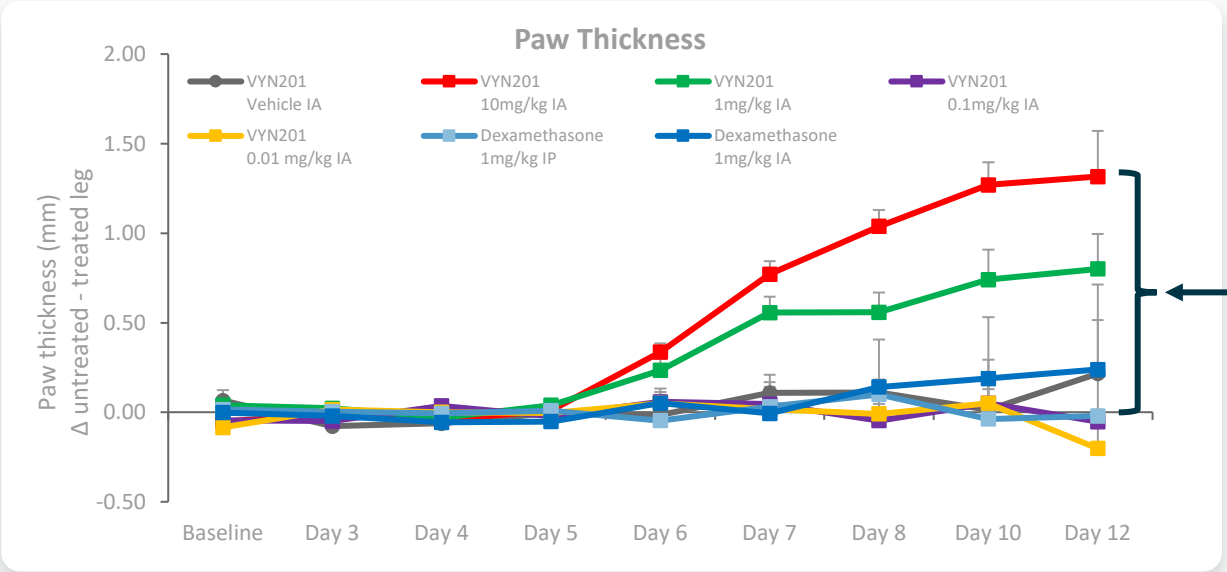
Marked inhibition of arthritis signs and symptoms for VYN201 at 1 & 10mg/kg dose levels with severity scores approaching "normal" (mean severity score <1)

*Scoring based on a five-point composite severity scale of redness, swelling of the ankles and wrists, and paw thickness. Scoring ranges from 0 (normal) to 4 (extensive signs and symptoms of arthritis);
CAIA = Collagen Antibody Induced Arthritis; IA = Intra-articular; IP = Intraperitoneal

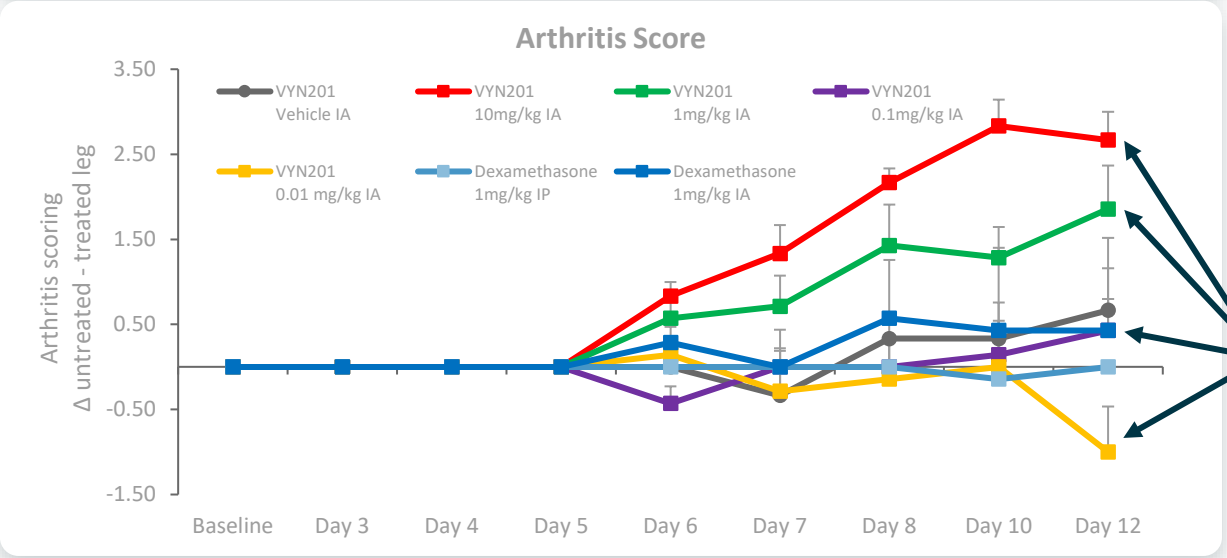
VYNE™ THERAPEUTICS

VYN201: CAIA Mouse Model of Arthritis – Systemic Impact

Demonstrated localized dose-dependent effect



VYN201 1 & 10mg/kg results demonstrated the highest localized effect in the treated limb when compared to the untreated limbs (largest delta between treated and untreated limbs)



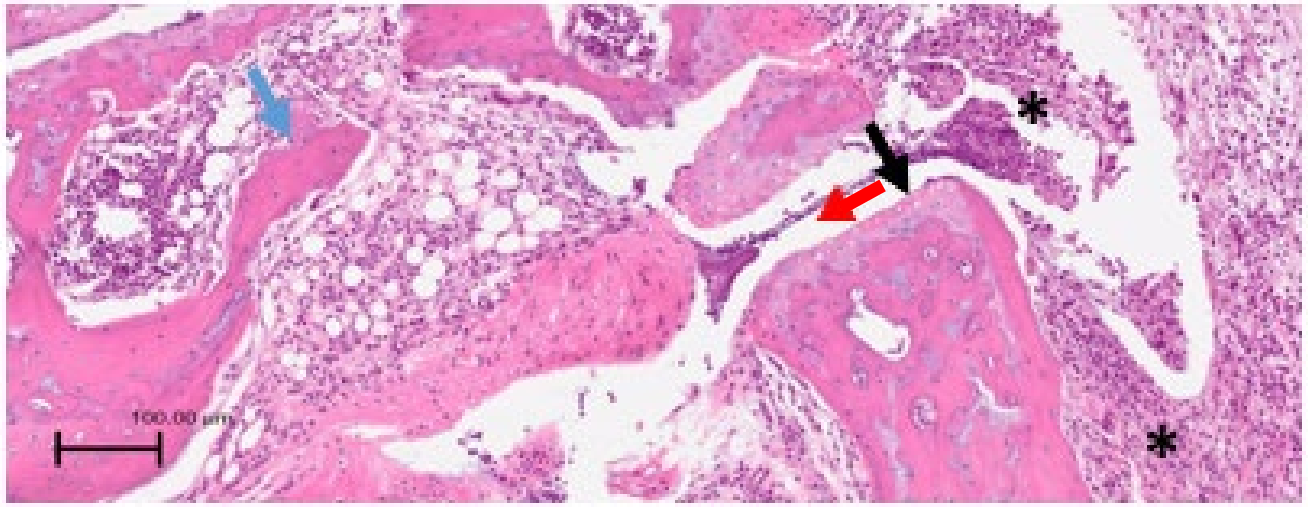
Treatment effect for VYN201 treated animals was dose-dependent over the dose range 0.01 to 10mg/kg

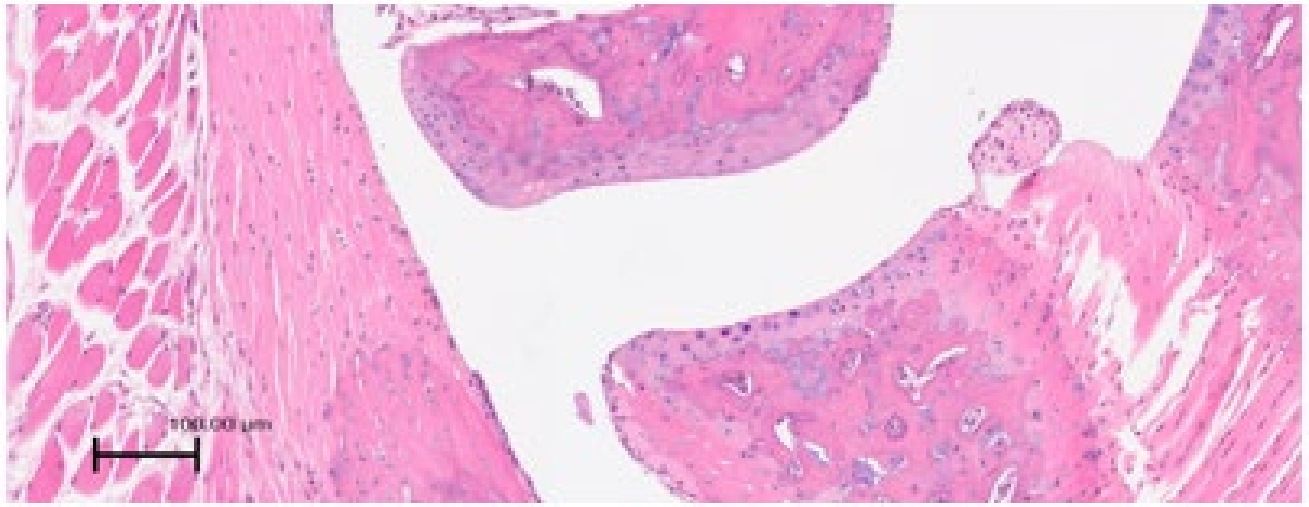
*Scoring based on a five-point composite severity scale of redness, swelling of the ankles and wrists, and paw thickness. Scoring ranges from 0 (normal) to 4 (extensive signs and symptoms of arthritis); CAIA = Collagen Antibody Induced Arthritis; IA = Intra-articular; IP = Intraperitoneal

VYN201: CAIA Mouse Model of Arthritis – Histopathology

Joint histopathology confirmed arthritis clinical scoring & local effect

Inflammation marked with asterisk; damage to bone marked with a blue arrow; inflammatory cells and cellular debris in the joint space marked with red arrow; damage to cartilage marked with black arrow; scale bar-100µm





VYN201 10mg/kg treatment group

Untreated right paw

- Arthritis score 4 "severe"
- Severe inflammation with destruction of both cartilage and bone

Treated left paw

- Arthritis score 0 "within normal limits"
- No evidence of inflammatory cell infiltrate in the joint spaces

NASDAQ: VYNE