UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): July 22, 2021

CORBUS PHARMACEUTICALS HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-37348**	**46-4348039**
(State or other jurisdiction of incorporation)	*(Commission File Number)*	*(IRS Employer Identification No.)*

500 River Ridge Drive, Norwood, MA	**02062**
(Address of principal executive offices)	*(Zip Code)*

Registrant's telephone number, including area code: **(617) 963-0100**

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	CRBP	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1 933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

Corbus Pharmaceuticals Holdings, Inc. is using the slides attached hereto as Exhibit 99.1 to this Current Report on Form 8-K in connection with management presentations to describe its business.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibit No.	Description
99.1	Investor Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CORBUS PHARMACEUTICALS HOLDINGS, INC.

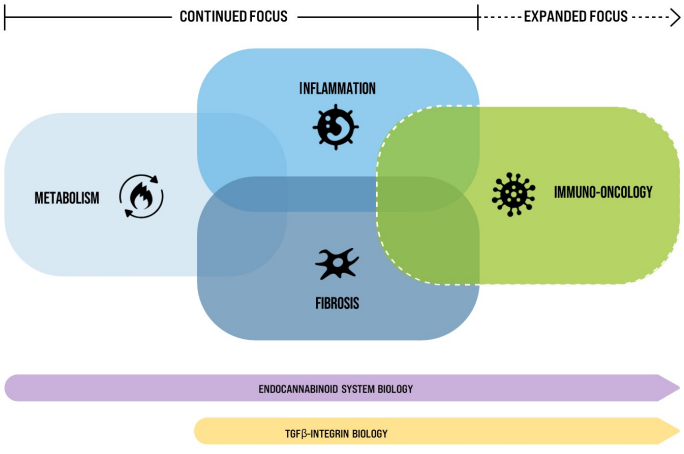
Dated: July 22, 2021

By: */s/ Yuval Cohen*
Name: Yuval Cohen
Title: Chief Executive Officer

FORWARD-LOOKING STATEMENTS

This presentation contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's restructuring, trial results, product development, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statements that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors, including the potential impact of the recent COVID-19 pandemic and the potential impact of sustained social distancing efforts, on our operations, clinical development plans and timelines, which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the Securities and Exchange Commission. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Expanding Our Therapeutic Focus



- Expertise across all phases of drug development
- Track record of executing complex global studies on time and on budget
- Funded through Q1 2024

A Diverse Pipeline with Multiple Shots on Goal

Compound	Therapeutic Areas / Indications	Preclinical	Phase 1	Phase 2	Phase 3
TARGETING THE ENDOCANNABINOID SYSTEM					
Lenabasum	Dermatomyositis* Lupus				
CB1 Inverse Agonists	Metabolism				
CB2 Agonists	Solid Tumors				
TARGETING THE TGFβ ACTIVATING INTEGRINS					
Anti-αvβ8 mAb	Solid Tumors				
Anti-αvβ6/αvβ8 mAb	Fibrosis				

*Topline results from DETERMINE study showed no significant differences in the primary or secondary endpoints.
CB1 = cannabinoid receptor type 1; CB2 = cannabinoid receptor type 2

PROGRAM 1:

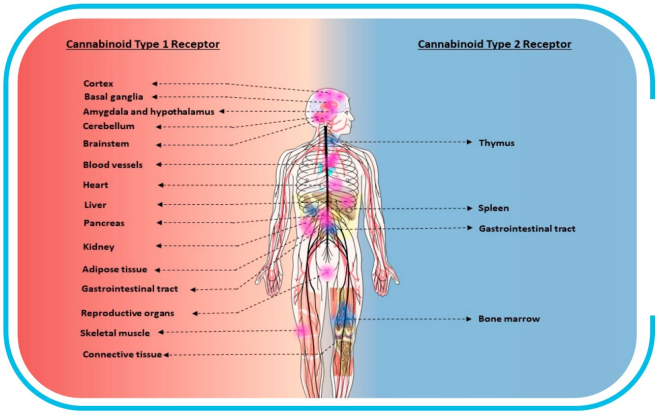
TARGETING THE ENDOCANNABINOID SYSTEM

Endocannabinoid System

2 GPCRs:
CB1 and CB2

2 endogenous agonists:
anandamide & 2-AG

Metabolic enzymes
FAAH and MAGL



Haspula, et al. *Cannabinoid Receptors: An Update on Cell Signaling, Pathophysiological Roles and Therapeutic Opportunities in Neurological, Cardiovascular, and Inflammatory Diseases.* International Journal of Molecular Sciences. 2020;21:5.

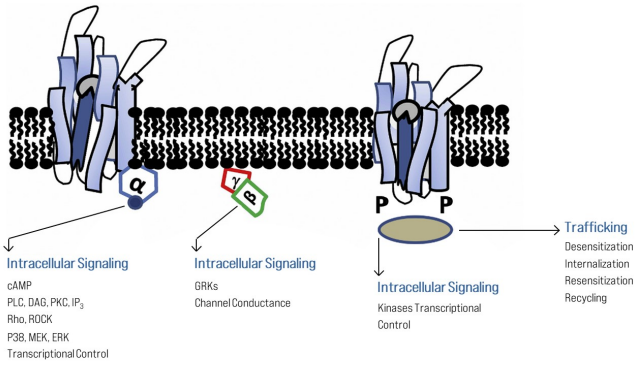
LENABASUM:
A LATE-STAGE CB2 AGONIST FOR AUTOIMMUNE DISEASES

Lenabasum: CB2 Agonist in Late-Stage Development

PURPOSE
Inflammatory and fibrotic diseases

INNOVATION
- First-in-class
- Targets activated immune cells
- Non-immunosuppressive
- Add-on to current therapies

MOA
- Activates resolution of inflammation
- Reduces levels of inflammatory mediators
- Inhibits fibrotic processes



Howlett, et al. *CB 1 and CB 2 Receptor Pharmacology.* Advances in Pharmacology. 2017;80:192.

Key Lenabasum Phase 2 and 3 Studies

Target (Program)	Phase	Number Dosed	Status
Dermatomyositis	3	175	• Primary efficacy endpoint (Total Improvement Score) not met • Additional data analyses being completed and preparing for discussions with FDA
SLE	2	102	• Ongoing, topline data expected second half of 2021
Systemic Sclerosis	3	363	• Primary efficacy endpoint (ACR CRISS score) not met • FVC changes seen in sub-population in post-hoc analysis • Acceptable safety profile • Analyzing data on FVC in conjunction with dermatomyositis data on FVC
Cystic Fibrosis	2b	525	• Primary efficacy endpoint (pulmonary exacerbation rate) was not met • Acceptable safety profile • Not planning additional studies in CF

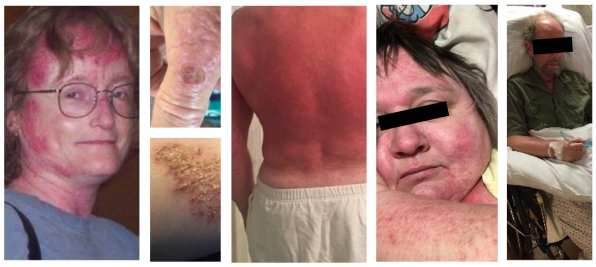
ACCEPTABLE SAFETY PROFILE IN STUDIES TO DATE, ~1,300 SUBJECTS HAVE RECEIVED LENABASUM

Most common adverse events related to lenabasum: Dizziness, headache, fatigue

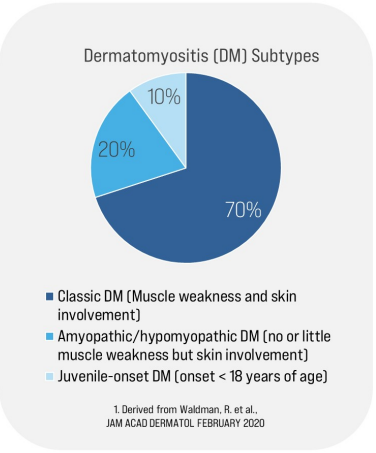
Dermatomyositis at a Glance

DERMATOMYOSITIS *der·mat·o·my·o·si·tis*

Chronic, rare, inflammatory, clinically heterogenous autoimmune diseases



Images provided by Myositis Support and Understanding and The Myositis Association.



1. Derived from Waldman, R. et al., JAM ACAD DERMATOL FEBRUARY 2020

Significant Unmet Need Remains for Treatment of Dermatomyositis

30% MORTALITY
in five years[2]

Affects
~ 80,000
People in North America, Europe and Japan[1,2]

CONDITION MAY BE FATAL IN ADULTS
due to severe muscle weakness, malnutrition, pneumonia and lung failure[3]

Typically treated with immunosuppressants and immunomodulating agents with **variable effectiveness and toxicity concerns**

1. Health Advances, LLC Analysis, 2. Schiopu et al, 2012, 3. NIH's U.S. National Library of Medicine

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Phase 3 DETERMINE Study Protocol

Double-blind, Randomized, Placebo-controlled study

Trial in adults with active classic dermatomyositis or amyopathic/hypomyopathic dermatomyositis

PRIMARY ENDPOINT

ACR & EULAR 2016 Total Improvement Score (TIS) in Adult Dermatomyositis and Polymyositis at Week 28, lenabasum BID vs. placebo (n = 175)

MULTINATIONAL

2:1:2 DOSING — Placebo | 5 mg BID | 20 mg BID

KEY SECONDARY ENDPOINTS

- Proportion of subjects who achieve Definition of Improvement (DOI)
- Change in Investigator Global Assessment (IGA) scale of skin activity
- Change in CDASI activity score

ORPHAN DRUG DESIGNATION FROM
FDA | EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

The timing of the primary efficacy endpoint was changed from Week 52 to Week 28 following developments in competitive landscape with studies that were shorter than one year using the same efficacy endpoint as DETERMINE.

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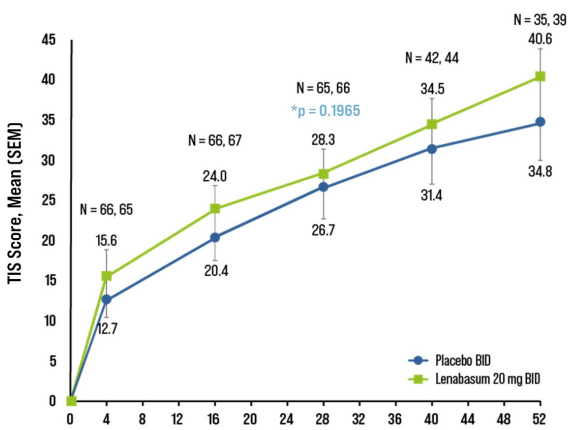
Phase 3 Study did not Meet Primary Endpoint of Total Improvement Score (TIS) at Week 28
Lenabasum was Associated with Higher TIS Compared to Placebo at all Timepoints



- Nominal p = 0.0795, lenabasum 20 mg twice daily (BID) group versus control, overall, visits Weeks 4-52, MMRM
- Lenabasum 20 mg BID showed greater treatment effect than 5 mg BID throughout

Fixed effects in MMRM were baseline MMT-8, treatment, region, visit, immunosuppressant use, treatment x visit, and treatment x immunosuppressant interaction

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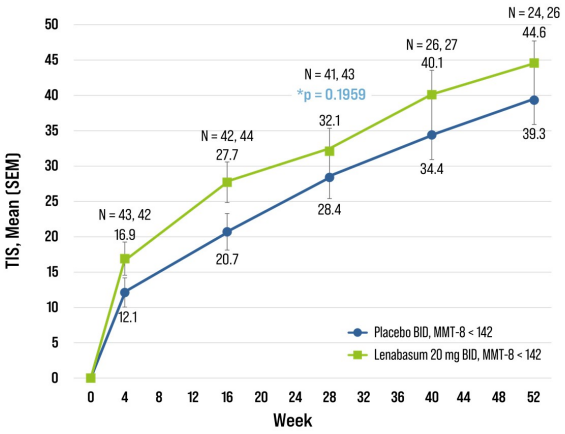
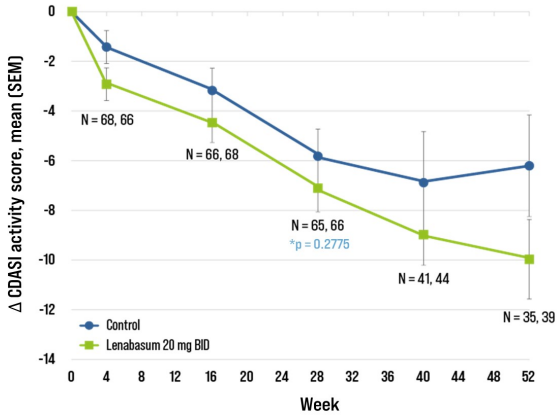
Highest Improvement in TIS Seen in Lenabasum-Treated Subjects with Muscle Weakness (MMT-8 < 142)



- Nominal p = 0.0302, lenabasum 20 mg twice daily (BID) group versus control, overall, visits Weeks 4-52, MMRM

Fixed effects in MMRM were treatment, visit, corticosteroid use, and treatment x visit interaction

Greater Improvement in CDASI Activity Scores Seen in Lenabasum Treated Subjects vs. Placebo

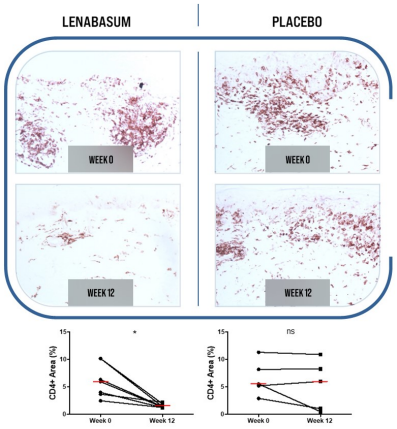


- Cutaneous Dermatomyositis Activity and Severity Index (CDASI) activity score is a validated outcome that was designed to assess inflammatory skin involvement
- Used as primary endpoint in positive lenabasum Phase 2 study (n = 22) in skin-predominant dermatomyositis
- Nominal p = 0.1083, lenabasum 20 mg twice daily (BID) group versus control, overall, visits Weeks 4-52, MMRM
- Greater overall visit improvement in CDASI activity scores was seen in subjects with skin involvement but no muscle weakness (MMT-8 = 150) who were treated lenabasum 20 mg versus the control, nominal p = 0.0166

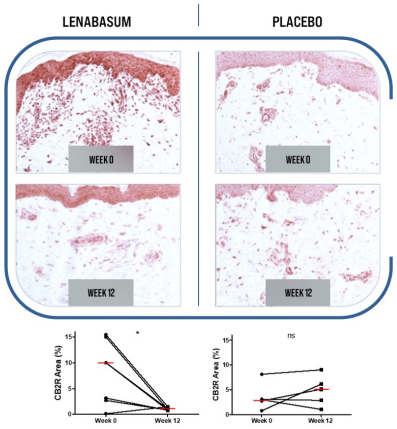
Fixed effects in MMRM were baseline CDASI, treatment, corticosteroid use, visit, baseline x visit, and treatment x visit interaction

Phase 2 Dermatomyositis Study Biomarkers: Lenabasum Treatment Reduced CD4 and CB2 Expression in Lesional Skin from Dermatomyositis Subjects

Lenabasum treatment was associated with reduction in CD4+ T cell infiltration in skin biopsies in DM



Lenabasum treatment was associated with reduction in CB2 in skin biopsies in DM



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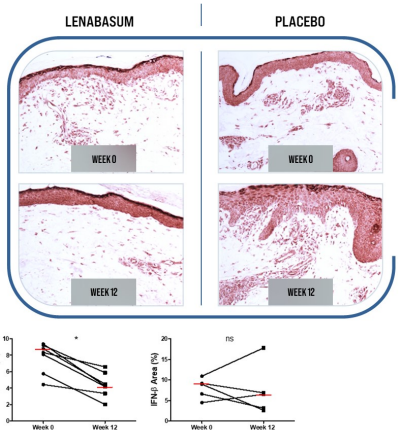
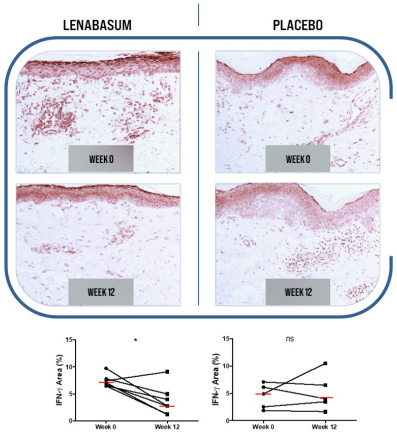
CD4 and CB2 expression were significantly decreased at week 12 versus baseline, $p < 0.05$, in paired biopsies of lesional skin from lenabasum-treated subjects, but not paired skin biopsies from placebo-treated subjects from the Phase 2 study of lenabasum in subjects with dermatomyositis. Source: Chen, ACR Abstract 2018

Phase 2 Dermatomyositis Study Biomarkers: Lenabasum Treatment Reduced Interferon-β and IFNγ Expression in Lesional Skin from Dermatomyositis Subjects

Lenabasum treatment was associated with reduction in interferon-β in skin biopsies in DM



Lenabasum treatment was associated with reduction in interferon-γ in skin biopsies in DM



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*IFN-β and IFNγ B2 expression were significantly decreased at week 12 versus baseline, $p < 0.05$, in paired biopsies of lesional skin from lenabasum-treated subjects, but not paired skin biopsies from placebo-treated subjects from the Phase 2 study of lenabasum in subjects with dermatomyositis. Source: Chen, ACR Abstract 2018

Competitive Landscape

Treatment	Target & Delivery	Company	Phase	Subjects	Endpoint
Lenabasum	CB2 agonist (oral)	CORBUS PHARMACEUTICALS	3 (Primary endpoint not met 2021)	175	**TIS**** at Week 28
octagam® 10%	IVIg	Pfizer	Approved 2021 (Primary endpoint met)	94	Number of patients who had an increase of ≥20 points on the **TIS** at 16 weeks
PF-06823859	IFNß1 Fibroblast blocker (IV)	Pfizer	2	76	**CDASI** Activity Score, change from baseline activity at Week 12
HiZentra (Immune Globulin Subcutaneous (Human)) 20% Liquid	IVIg	CSL Behring Biotherapies for Life™	3	126	Responder Rate: **TIS** >=20 at week 25 and one prior visit (wk 17 or 21)
ORENCIA® (abatacept)	CTLA-4 (IV/SC)	Bristol-Myers Squibb	3	150	Number of subjects who achieve DDI** at Week 24
Stelara® (ustekinumab)	IL-12 & 23 (IV/SC)	Johnson & Johnson	3 (Japan only)	50	Percentage of Participants who achieve Minimal Improvement in **TIS** at Week 24
KZR-616	Selective Immuno-protenasome Inhibitor (SC)	KEZAR LIFE SCIENCES	2	24	Mean change in **TIS** at 16 weeks
ACTEMRA® tocilizumab	IL-6 (IV)	Genentech A Member of the Roche Group	2 (Primary endpoint not met 2020)	36	Compare the Average **TIS** at Visits 2 Through 7 During the 6-month Treatment Period Between the Treatment and Placebo Arms [Time Frame: Week 4, 8, 12, 16, 20, and 24]

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**TIS = Total Improvement Score
DDI = Definition of Improvement

Systemic Lupus Erythematosus (SLE): Topline Phase 2 Study Results Expected 2H 2021

NIH

STUDY FUNDED AND MANAGED BY THE AUTOIMMUNITY CENTERS OF EXCELLENCE AT THE NATIONAL INSTITUTES OF HEALTH

PRIMARY ENDPOINT:

- Mean 7-day average maximum daily pain numerical rating score (NRS) at 12 weeks, n = 101

KEY SECONDARY ENDPOINTS:

- SLE Responder Index
- SELENA SLEDAI
- BILAG 2004

SLE AFFECTS **+200,000 PEOPLE** *IN THE U.S.*

Izmirly, et al. *Prevalence of Systemic Lupus Erythematosus in the United States: Estimates from a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries.* Arthritis & Rheumatology. 2021; Epub ahead of print.

2ND GENERATION CB1 INVERSE AGONISTS FOR METABOLIC AND FIBROTIC DISEASES

Obesity is a Growing Health Crisis in the U.S.

Currently **33%** of the U.S. population is obese and it is estimated to rise to **~50% by the end of the decade**[1]

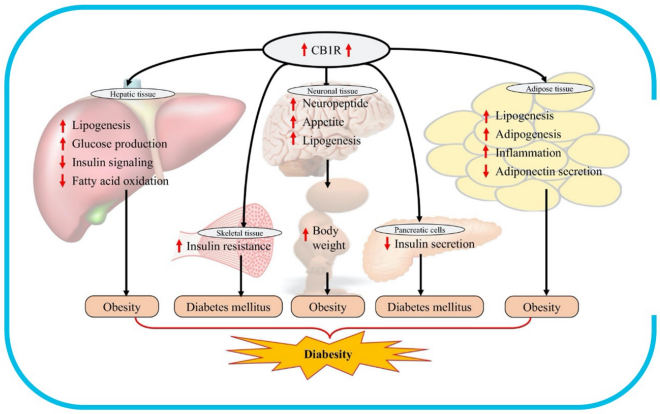
Obese patients are **2 X MORE LIKELY** to develop hypertension, dementia and certain cancers [2]

Obese patients are over **3 X MORE LIKELY** to develop diabetes, osteoarthritis and end stage renal disease [2]

~ $480B of annual direct medical costs in the US are attributed to obesity [2]

[1]Ward et al, Projected U.S. State-Level Prevalence of Adult Obesity and Severe Obesity, NEJM, Dec. 2019 | [2]Milkin Institute October 2018

CB1 Activation Contributes to "Diabesity"



CB1 ACTIVATION INCREASES:
- Appetite
- Food intake
- Fat production and storage
- Insulin resistance
- Inflammation
- Fibrosis

CB1 ACTIVATION DECREASES:
- Insulin secretion
- Fat oxidation
- Energy expenditure

Deeba, et al. *Targeting the endocannabinoid system in diabesity: Fact or fiction?* Drug Discovery Today. 2021in press2.

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CB1 is a Validated Target in Metabolic Diseases

SEVERAL FIRST GENERATION CB1 INVERSE AGONISTS ADVANCED TO LATE-STAGE CLINICAL DEVELOPMENT

SANOFI

Pfizer
Otenabant

Bristol Myers Squibb
Ibipinabant

MERCK
Taranabant

ACOMPLIA
Rimonabant

Rimonabant

- Approved in EU and launched in 2006 for treatment of obesity and other metabolic-related parameters
- Withdrawn in 2008 for depression and suicidality related to rimonabant binding to CB1 in the brain
- Drug class abandoned

SECOND GENERATION OF CB1 INVERSE AGONISTS AIM TO MAINTAIN POTENCY BUT MINIMIZE CB1 BINDING IN BRAIN

*Pfizer, Bristol Myers Squibb, and Merck were in clinical trials. Trials were terminated due to rimonabant withdrawal.

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CB1 Inverse Agonist Program

PURPOSE

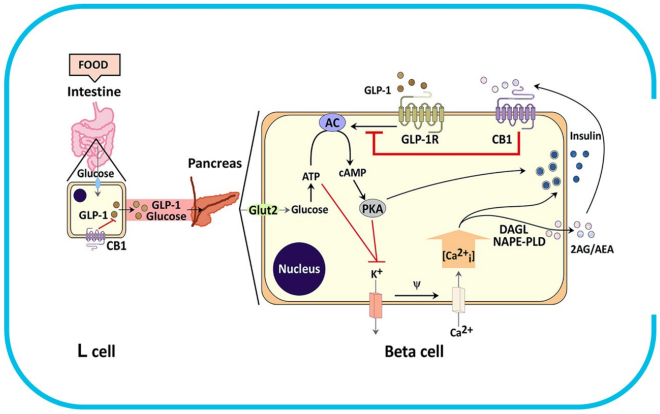
- Obesity, diabetes/diabetic nephropathy, NASH

INNOVATION

- Second generation small molecule with limited brain levels to increase safety
- Potential to augment effects of GLP-1R agonists in diabetes and obesity
- Potential to preserve renal function

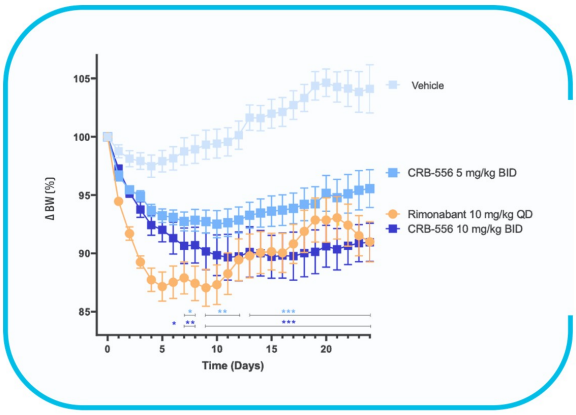
MOA

- Reduces appetite, food intake, lipogenesis, dyslipidemia, inflammation
- Increases insulin sensitivity and secretion



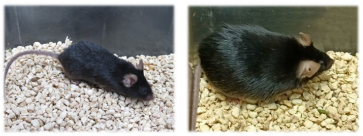
González-Mariscal, et al. *Blockade of cannabinoid 1 receptor improves GLP-1R mediated insulin secretion in mice.* Molecular and Cellular Endocrinology. 2016;423:1-10.
Neurological, Cardiovascular, and Inflammatory Diseases. International Journal of Molecular Sciences. 2020;21:5.

DIO Model: CRB-556 Induces Weight Loss in Obese Mice



Mice received a high-fat diet for 14 weeks to induce obesity and glucose intolerance prior to testing, then continued to receive high-fat diet while receiving test compounds. Vehicle is CRB-556 control. Day 0 is start of dosing with test compounds. N = 10 mice per time point per dose of compound.

- CB1 inverse agonist CRB-556 induced dose-dependent weight loss in mice with diet-induced obesity
- Effect similar to rimonabant

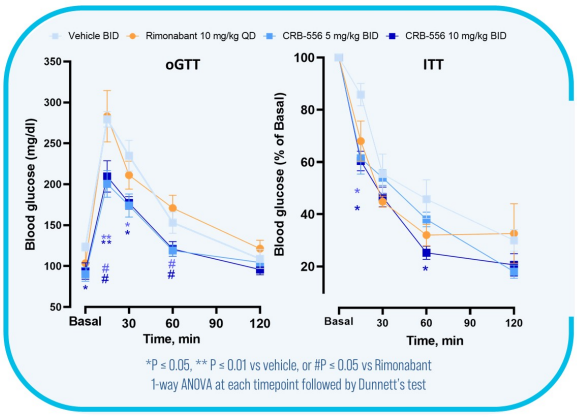


Chow diet | High fat diet

Note, mice pictured were not treated with CRB-556.
Photos are courtesy of GVK-Aragen.

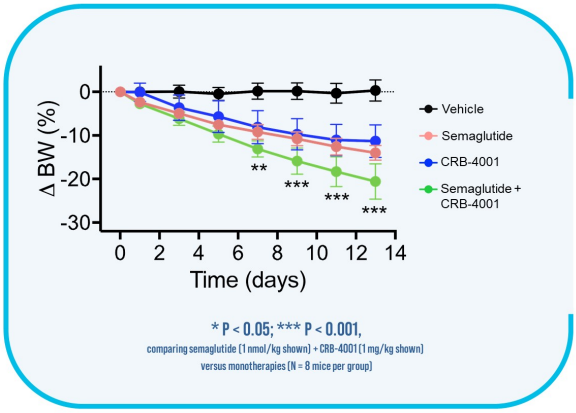
DIO Model: CRB-556 Improves Glucose Tolerance and Insulin Sensitivity in Obese Mice

CRB-556 improved glucose tolerance and insulin sensitivity in mice with diet-induced obesity, similar to rimonabant



Mice received a high-fat diet for 14 weeks to induce obesity and glucose intolerance prior to testing, then continued to receive high-fat diet while receiving test compounds for 28 days. Vehicle is CRB-556 control. Day 0 is start of dosing with test compounds. Oral glucose challenge (2 g/kg, post overnight fast) and insulin sensitivity testing (2 U/kg Humulin IP, post 6 hour fast) were done on Day 25, 1 hr 45 min after morning dose. N = 5 mice per time point per dose of compound

CRB-4001 Augments Weight Loss Provided by Semaglutide in Obese Mice

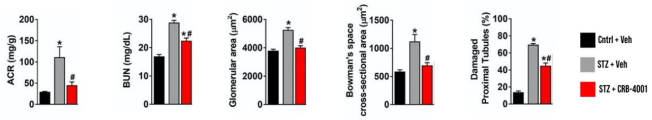


- CB1 inverse agonist CRB-4001 augmented semaglutide-induced weight loss in obese mice and insulin sensitization (improved basal glucose levels and glucose disappearance rate)
- Wegovy™ approved for chronic weight management by FDA on June 4, 2021*

ONCE-WEEKLY wegovy™ semaglutide injection 2.4 mg

Graph: Zizzari, et al. *CB1 and GLP-1 Receptors Cross Talk Provides New Therapies for Obesity.* Diabetes. 2021;70:421.
*FDA. (2021, June 4) *FDA Approves New Drug Treatment for Chronic Weight Management, First Since 2014* [Press release] https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treatment-chronic-weight-management-first-2014

CRB-4001 Improves Renal Structure Function in a Model of Diabetic Nephropathy



#P < 0.05 relative to the corresponding streptozotocin (STZ) group treated with vehicle (Veh)

C57Bl/6 mice with STZ-induced diabetic nephropathy were treated for 16 weeks with 3 mg/kg CRB-4001. Compared to the STZ group treated with vehicle.

CRB-4001 INCREASED:

- Preservation of renal structure

CRB-4001 DECREASED:

- GLUT2 expression and translocation to basal membrane
- Blood urea nitrogen (BUN)
- Albumin to creatinine ratio (ACR)
- Inflammatory mediators
- Tubulo-interstitial fibrosis

Hinden, et al. *Modulation of Renal GLUT2 by the Cannabinoid-1 Receptor: Implications for the Treatment of Diabetic Nephropathy.* Journal of the American Society of Nephrology. 2018;29:436-446.

Select Corbus CB1 Inverse Agonists Have Low Brain Drug Levels and Receptor Occupancy with Repeated Dosing in Mice

Compound	C_{max} Brain: Plasma (Ratio, Range)	AUC_{0-24} Brain: Plasma (Ratio, Range)	CB1 Receptor Occupancy in Brain, Chronic Dosing, 10-20 mg/kg	Comment
Rimonabant (Sanofi)	0.90 - > 1	–	Upper limit of quantification	Single IP dose[1]
CRB-4001*	0.06-0.07	0.49-0.83	Lower limit of quantification[2]	Accumulates in brain with repeated dosing
CRB-556**	0.01-0.03	0.04-0.07	Lower limit of quantification	Minimal accumulation
CRB-545**	0.01-0.04	0.03-0.08	Lower limit of quantification	No accumulation
CRB-625**	0.00-0.002	0.00-0.01	Not determined	No accumulation

29

*We are not continuing development of CRB-4001. **Current candidates under evaluation for potential clinical development

1. Han, et al. *A novel peripheral cannabinoid 1 receptor antagonist, AJ5012, improves metabolic outcomes and suppresses adipose tissue inflammation in obese mice*. FASEB J. 2019; 33:4314-4326.
2. Tam, et. al. *Peripheral cannabinoid-1 receptor inverse agonism reduces obesity by reversing leptin resistance*. Cell Metab. 2012; 16:167-79

NEW DRUG CLASS:

CANNABINOID RECEPTOR AGONISTS FOR SOLID TUMORS

30

CB2 Agonist Immuno-oncology Program

PURPOSE

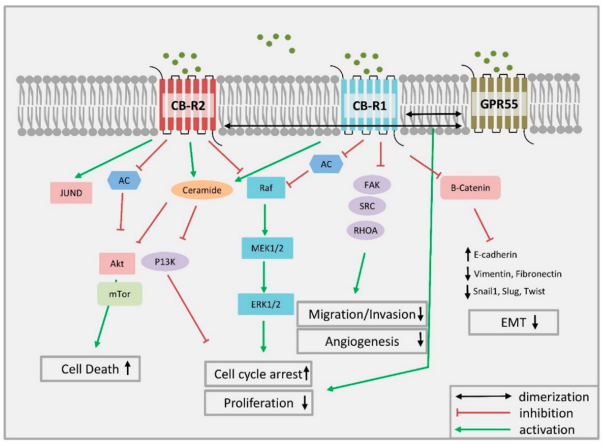
Solid tumors in combination with standard treatments including checkpoint inhibitors

INNOVATION

- First-in-class
- Affects both tumor cells and immune system
- Potential to augment effects of CPIs

MOA

- Inhibits cell cycle progression
- Inhibits cell proliferation
- Induces apoptosis
- Reduces angiogenesis
- Reduces epithelial-mesenchymal transformation
- Inhibits cell cycle progression



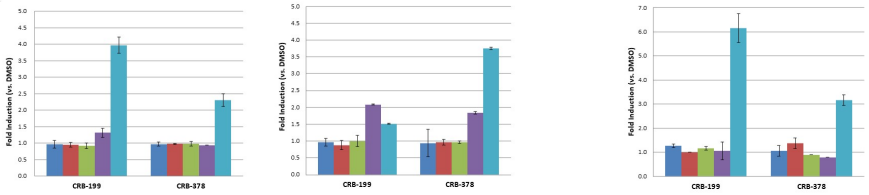
Kiskova, et al. *Future Aspects for Cannabinoids in Breast Cancer Therapy*. International Journal of Molecular Sciences. 2019;20:5.

Corbus CB2 Agonists Reduce Cancer Cell Viability by Promoting Apoptosis

Inhibition of cancer cell viability, IC50 (μM)

Compound	HER2+ Breast Cancer			Triple Negative Breast Cancer			ER+ Breast Cancer		Glioblastoma	
	BT474	HCC1954	SKBR3	MDA-MB-468	MDA-MB-231	MDA-MB-436	T-47D	MCF7	SF126	U251
CRB-199*	4.5	3.5	5.2	3.1	5.4	4.0	5.4	>10	9.0	3.8
CRB-378*	8.0	6.4	10.5	3.6	8.4	4.0	10.4	13.8	18.5	3.5

*Current candidates under evaluation for potential clinical development

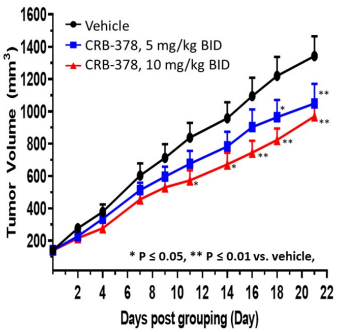


Fold-induction of caspases 3 and 7 vs. vehicle (non-cytotoxic concentrations)

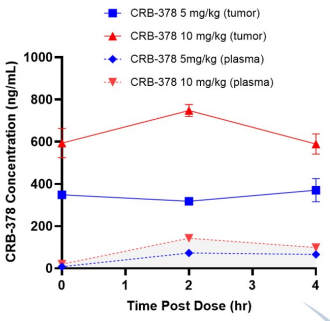
Concentrations (μM) 20.0 6.7 2.2 0.7 0.2

CRB-378 Has Single Agent Activity in HCC1954 Her2+ Breast Cancer Xenograft Model

CRB- 378 REDUCES TUMOR VOLUME



CRB- 378 IS CONCENTRATED IN THE TUMOR

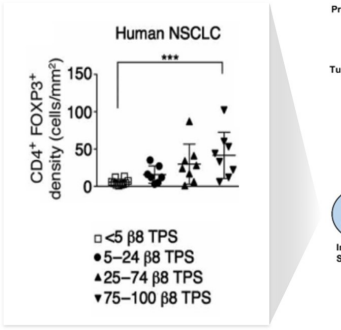


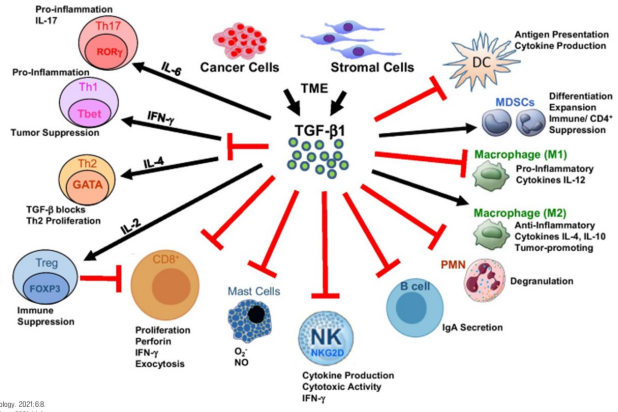
Female Balb/c mice nude mice were injected in the flank with HCC1954 Her2+ breast cancer cells. Pharmacological treatments for 21 days were started when tumors reached 90-180 mm3 were cultured with vehicle or CRB-378 for different times. Tumor size was measured using a caliper and tumor volume was calculated. Concentration of CRB-378 in plasma and tumors was determined on Day 21 by LC-MS/MS.

PROGRAM 2:

TARGETING TGFβ ACTIVATING INTEGRINS

Immune Evasion is Mediated by TGFβ in Late-Stage Tumors

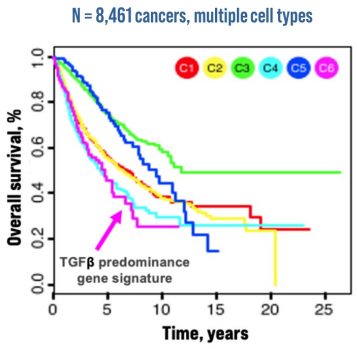




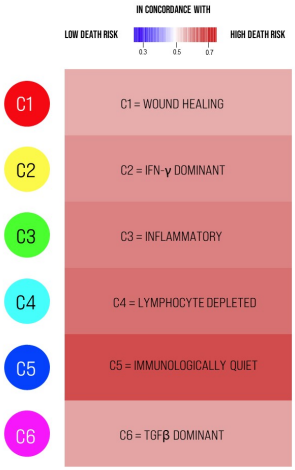
Seed, et al. *A tumor-specific mechanism of T reg enrichment mediated by the integrin αvβ8.* Science Immunology. 2021;6:8.
Kim, et al. *Novel therapies emerging in oncology to target the TGF-β pathway.* Journal of Hematology & Oncology. 2021;14:4.

Treg numbers are increased in human non-small lung cell cancers in proportion to number of cancer cells expressing β8 (TPS)

Lower Survival in Patients with High TGFβ Tumor Gene Signature



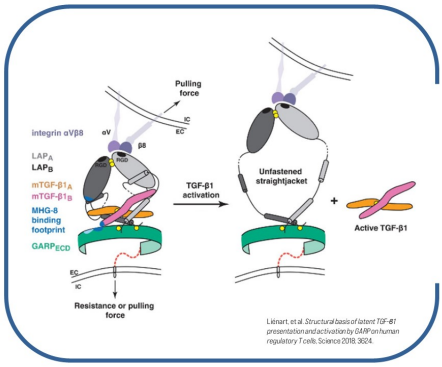
Strong concordance between TGFβ immune expression signature score and overall survival for each immune subtype of tumor



Thorsson, et al. *The Immune Landscape of Cancer*. Immunity. 2018. 48:817

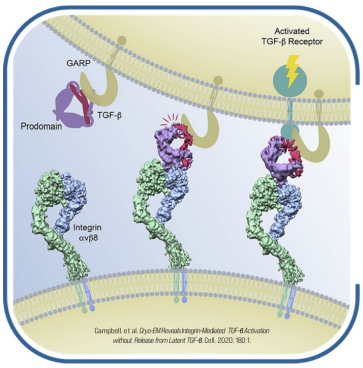
αvβ8 on Tumor Cells Activates TGFβ

DIFFUSIBLE ACTIVE TGFβ



Lienart, et al. *Structural basis of latent TGF-β1 presentation and activation by GARP on human regulatory T cells*. Science 2018; 3624.

NON-DIFFUSIBLE ACTIVE TGFβ



Campbell, et al. *Oyo-EM Reveals Integrin-Mediated TGF-β Activation without Release from Latent TGF-β*. Cell. 2020; 180:1.

Non-diffusible TGFβ may be most relevant form of active TGFβ in cancer

Drug Development of Inhibitors of TGFβ-Activating Integrins

MONOCLONAL ANTIBODY
SMALL MOLECULE

	ONCOLOGY		FIBROSIS	
	PHASE (DISCLOSED INDICATION)	TARGET	PHASE (DISCLOSED INDICATION)	TARGET
Pfizer	Phase 1 Solid tumors	αvβ8 (Y)	-	-
PLIANT	Preclinical	αvβ8 (●)	Phase 2 IPF & PSC	αvβ6/1 (●)
MORPHIC THERAPEUTIC	Preclinical	αvβ8 (●)	Preclinical	αvβ1 (●)
VENN THERAPEUTICS	Preclinical	αvβ8 (Y)	Preclinical	αvβ8/6 (Y)
AstraZeneca	-	-	Phase 1 CKD	αvβ8 (Y)
PLIANT NOVARTIS	-	-	Phase 1 NASH	αvβ1 (●)
abbvie MORPHIC THERAPEUTIC	-	-	Preclinical	αvβ6 (●)

CRB-601: Anti-αvβ8 mAb for Solid Tumors

PURPOSE

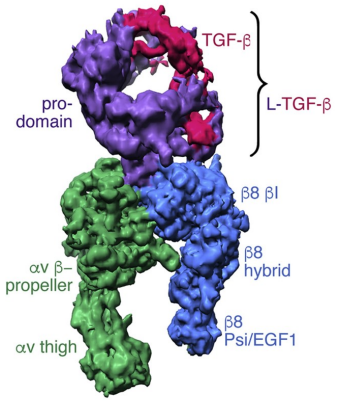
Treatment of solid tumors, in combination with standard treatments including checkpoint inhibitors

INNOVATION

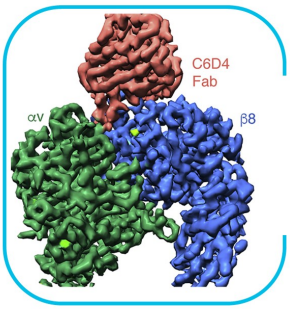
- Anti-αvβ8 mAb from Nishimura lab (UCSF)
- Genealogy: mC6D4 > hC6D4 > CRB-601
- Potential to augment effects of CPIs

MOA

- Binds with high affinity to block RGD-binding site of αvβ8
- Inhibits activation of diffusible and non-diffusible forms of TGFβ, at ~30-fold lower concentrations than 1st gen C6D4 mAb



TGFβ binding to αvβ8



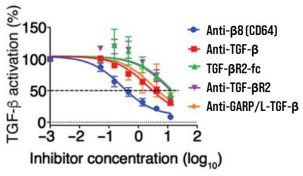
mC6D4 binding to αvβ8

Campbell, et al. *Cryo-EM Reveals Integrin-Mediated TGF-β Activation without Release from Latent TGF-β.* Cell. 2020; 180:491-493.

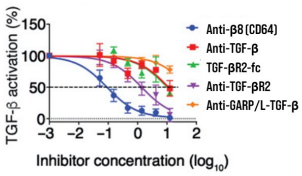
C6D4 (Precursor mAb Of CRB-601) Inhibits Activation of Both Diffusible and Non-Diffusible TGFβ

Inhibition of Activation of:

Diffusible TGFβ

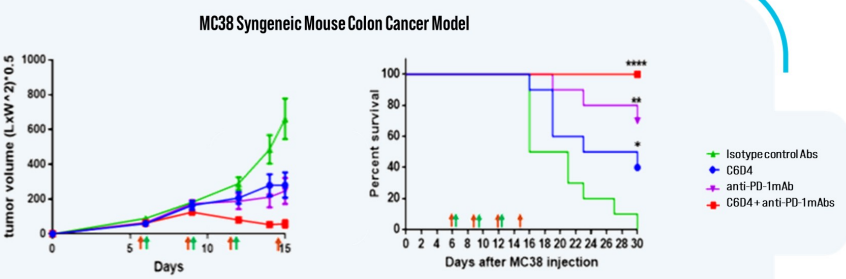


Non-Diffusible TGFβ



Seed, et al. *A tumor-specific mechanism of T reg enrichment mediated by the integrin αvβ8.* Science Immunology. 2021; 6:7.

C6D4 (Precursor mAb Of CRB-601) Augments Activity of Anti-PD-1 mAb

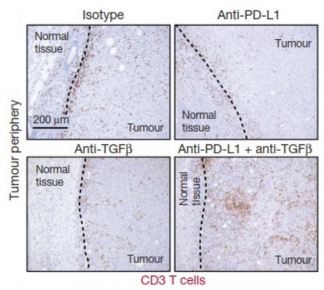


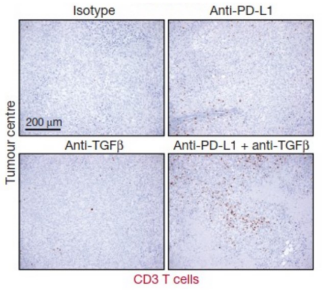
* P , 0.05, ** P < 0.01, **** P < 0.0001, vs. isotype control mAbs

C57Bl/6 mice were inoculated with MC38 cells, n = 10 per group. C6D4 (7 mg/kg) and anti-PD-1 (RMP1-14, 20 mg/kg) were administered on days 7, 10, 13, and 16.

Takasaka, et al. *Integrin αvβ8-expressing tumor cells evade host immunity by regulating TGF-β activation in immune cells.* JCI Insight. 2013;3:3.

Blocking Both TGFβ and PD-1 Augments T Cell Infiltration in Tumors

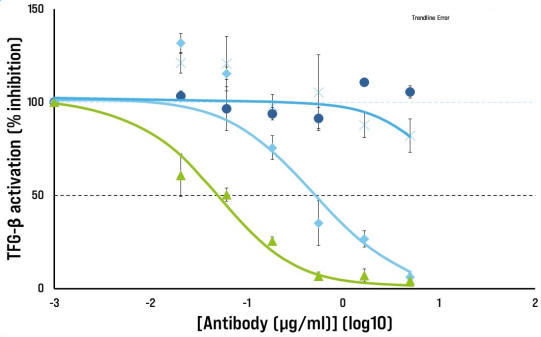




- Majority of infiltrating cells are CD8+ T cells
- Consistent with lessening immunosuppression
- CRB-601 + anti-PD-1 mAb have the potential to provide superior relief of immunosuppression

Mariathasan, et al. *TGFβ attenuates tumour response to PD-L1 blockade by contributing to exclusion of T cells.* Nature. 2018;554:547.

CRB-601 is Highly Effective at Inhibiting αvβ8-mediated TGFβ Activation In Vitro

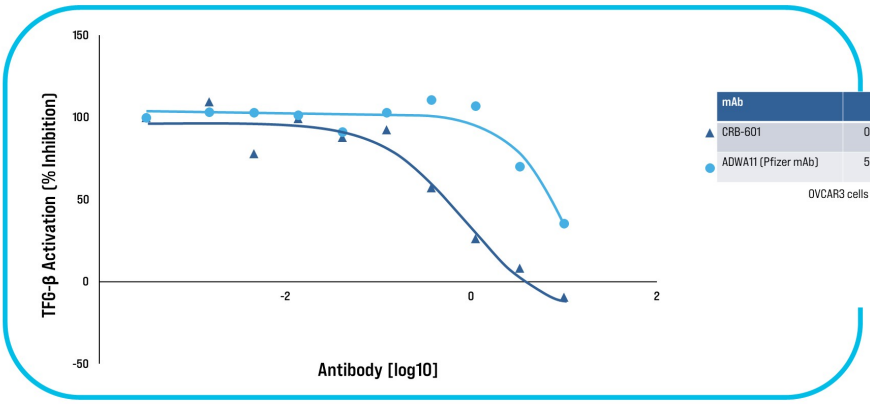


mAb	IC50
Antibody control	N/A
Anti-TGFβ mAb	21.85 µg/ml
Precursor mAb of CRB-601 (C6D4)	0.55 µg/ml
CRB-601	0.05 µg/ml

TML cells

Nishimura, S.L., Cormier, A., Ito, S., Lou, J., Marks, J.D., Cheng, Y., Campbell, M.G., Baron, J.L. (2021). Antibodies that bind integrin avb8 and uses thereof. *Patent Cooperation Treaty Pub. No. US2021013720.* Geneva, Switzerland. World Intellectual Property Organization.

CRB-601 Appears to be Significantly More Effective In Vitro at Inhibiting TGFβ than Equivalent Pfizer mAb



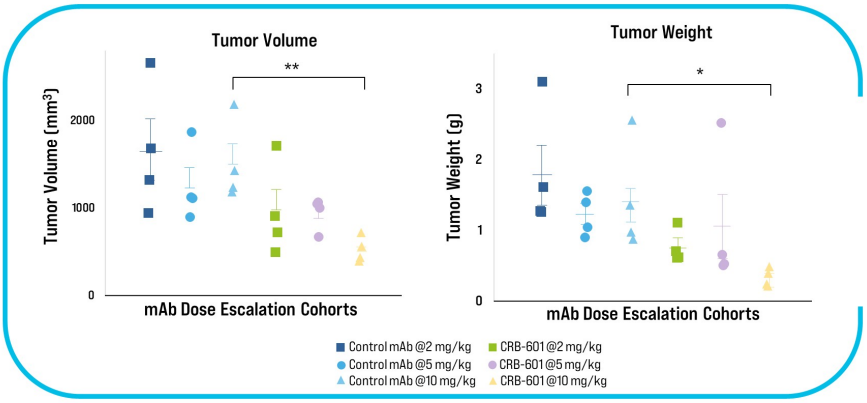
mAb	IC50
CRB-601	0.75 µg/ml
ADWA11 (Pfizer mAb)	57.7 µg/ml

OVCAR3 cells

Nishimura, S.L., Cormier, A., Ito, S., Lou, J., Marks, J.D., Cheng, Y., Campbell, M.G., Baron, J.L. (2021). Antibodies that bind integrin avb8 and uses thereof. *Patent Cooperation Treaty Pub. No. US2021013720.* Geneva, Switzerland. World Intellectual Property Organization.

CRB-601 Has Single Agent Effect in Syngeneic Lung Cancer Tumor Animal Model

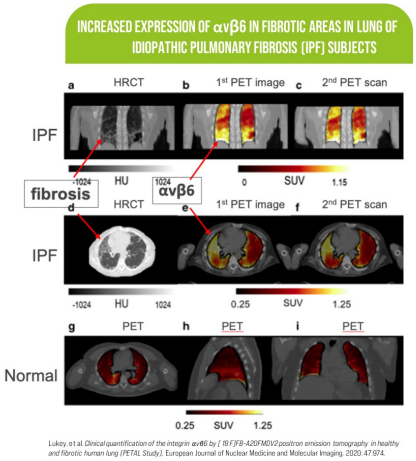
Syngeneic model: Lewis lung carcinoma



* Student's unpaired t-test, $p < 0.05$
** Student's unpaired t-test, $p < 0.01$

Nishimura, S.L., Cormier, A., Ito, S., Lou, J., Marks, J.D., Cheng, Y., Campbell, M.G., Baron, J.L. (2021). Antibodies that bind integrin avb8 and uses thereof. *Patent Cooperation Treaty Pub. No. US2021013720.* Geneva, Switzerland. World Intellectual Property Organization.

CRB-602: Anti-αvβ6/8 mAb for Fibrosis and Cancer



Lukey, et al. *Clinical quantification of the integrin avB6 by [18 F]FB-A20FMDV2 positron emission tomography in healthy and fibrotic human lung (PETAL Study).* European Journal of Nuclear Medicine and Molecular Imaging. 2020. 47:974.

- Licensed from by Panorama Research Inc.
- αvβ6 integrin also activates TGFβ
- αvβ6 is expressed in high levels on tumors of epithelial origin (carcinomas)
- αvβ6 is also expressed on epithelial cells in fibrotic diseases and thought to play an important role in lung, liver, biliary, and kidney fibrosis
- αvβ6 is more highly expressed in fibrotic areas in lungs of IPF subject than in non-fibrotic areas or normal lungs
- Antibody that targets both αvβ6 and αvβ8 may be useful in treatment of certain carcinomas
- Corbus anti-αvβ6/8 mAb will be tested in animal models of cancer and fibrosis, with estimated Phase 1 start by end of 2022

Expected Clinical Milestones 2021-2022

PROGRAM	MILESTONE	H2 2021	H1 2022	H2 2022
LENABASUM IN SYSTEMIC LUPUS ERYTHEMATOSUS	PHASE 2 DATA	✓		
CB1 INVERSE AGONISTS IN METABOLIC DISEASES	PHASE 1		✓	
CB2 AGONIST IN SOLID TUMORS	PHASE 1			✓
CRB-601 IN SOLID TUMORS (anti-αvβ8 mAb)	PHASE 1			✓
CRB-602 IN FIBROSIS (anti-αvβ6/8 mAb)	PHASE 1			✓

FINANCIAL PROFILE:
CRBP (NASDAQ)

125M Common Shares Outstanding (140.1M Fully Diluted)

$125M Cash Balance as of 3.31.2021

A Team with a Proven Record of Execution

Yuval Cohen, PhD
Chief Executive Officer, Director
Executive leadership experience in inflammatory disease drug

Sean Moran, CPA, MBA
Chief Financial Officer
Senior financial experience with emerging biotechnology, drug delivery and medical device companies

Craig Millian, MBA
Chief Commercial Officer
Experience leading commercial organizations and building successful brands at multiple biopharma companies

Barbara White, MD
Chief Medical Officer and Head of Research
Previous academician with industry, clinical development, and medical affairs experience in inflammatory and autoimmune diseases

Ross Lobell
VP, Regulatory Affairs
Regulatory affairs experience with an extensive biopharmaceutical background in leading preclinical, clinical and nonclinical regulatory strategies

Dylan Wenke
Head, Business Development
Experience leading corporate development, partnerships, and collaborations at pharmaceutical and venture-backed startups

An Experienced and Engaged Board of Directors

Amb. Alan Holmer Ret.
Chairman of the Board
More than two decades of public service in Washington, D.C. including Special Envoy to China; Former CEO of PhRMA

Avery W. (Chip) Catlin
Director
More than 25 years of senior financial leadership experience in life science companies; Former CFO and Secretary of Celldex Therapeutics

Yuval Cohen, PhD
Chief Executive Officer, Director
More than 13 years of executive leadership experience in inflammatory disease drug development

Rachelle Jacques
Director
More than 25-year professional career, experience in U.S. and global biopharmaceutical commercial leadership, including multiple high-profile product launches in rare diseases; CEO of Enzyvant Therapeutics

John K. Jenkins, MD
Director
Distinguished 25-year career serving at the U.S. FDA, including 15 years of senior leadership in CDER and OND

Pete Salzmann, MD, MBA
Director
20 years of industry experience and currently serves as Chief Executive Officer of Immunovant (NASDAQ: IMVT), a biopharmaceutical company focused on developing therapies for patients with autoimmune diseases

RESOLVE-1 Phase 3 in Systemic Sclerosis

Largest ever study in diffuse cutaneous systemic sclerosis (n=365, 52-weeks, 76 global sites)

First in a group of studies to allow patients to remain on background immunosuppressant therapy (IST)

RESULTS
Study did not meet primary endpoint

KEY LEARNINGS
Under-appreciated benefit from IST (especially in newly diagnosed patients) led to much higher improvement in the control group than anticipated

PRIMARY EFFICACY ENDPOINT: MEDIAN ACR CRISS SCORES AT WEEK 52

Visit 11 (Week 52)	Lenabasum 20 mg BID · N = 120	Lenabasum 5 mg BID · N = 120	Placebo N = 123
n	100	113	115
Mean (SD)	0.598 (0.432)	0.575 (0.423)	0.636 (0.422)
Median (Q1, Q3)	0.888 (0.061, 0.997)	0.827 (0.070, 0.988)	0.887 (0.071, 0.999)
p-value (Ranked Score, MMRM)	0.497	0.349	-

There were also no significant differences among treatment groups for the secondary efficacy outcomes.

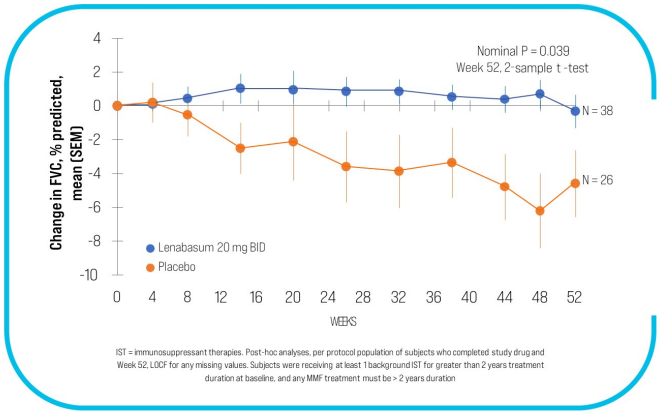
mITT population, primary efficacy analysis. MMRM with imputed values for missing core items, except LOCF for core items missing because of COVID-19.

NEXT STEPS: PREPARING THE RESOLVE-1 STUDY DATA FOR PUBLICATION AND WILL DECIDE ON THE NEXT STEPS IN THE DEVELOPMENT PROCESS PENDING THE OUTCOME OF THE DETERMINE STUDY.

PHASE 3 · Subjects Treated With Lenabasum 20 mg BID Added to Established IST (> 2 Year Duration) Had Stable FVC % Predicted

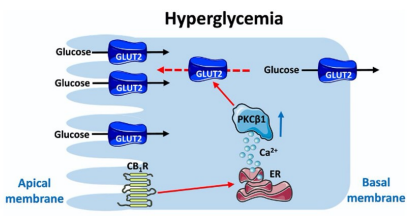
POST-HOC ANALYSES

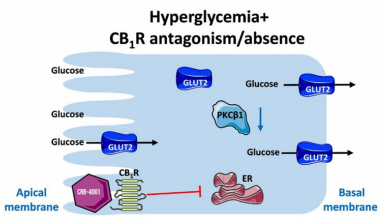
Subjects treated with lenabasum 20 mg BID added to established immunosuppressant therapies (IST) had stable FVC % predicted over 1 year



IST = immunosuppressant therapies. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and any MMF treatment must be > 2 years duration

CRB-4001 Acts In a Variety of Key Metabolic Pathways





Hinden, et al. *Modulation of Renal GLUT2 by the Cannabinoid-1 Receptor: Implications for the Treatment of Diabetic Nephropathy*, Journal of the American Society of Nephrology, 2018;29:436-446.