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): November 10, 2020

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 2.02. Results of Operations and Financial Condition.

Corbus Pharmaceuticals Holdings, Inc. (the "Company") issued a press release on November 10, 2020, disclosing financial information and operating metrics for its fiscal quarter ended September 30, 2020 and discussing its business outlook. A copy of the Company's press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 7.01. Regulation FD Disclosure.

See "Item 2.02 Results of Operations and Financial Condition" above.

The Company is using the slides attached hereto as Exhibit 99.2 to this Current Report on Form 8-K in connection with management presentations to describe additional data from its RESOLVE-1 Phase 3 study of lenabasum for the treatment of systemic sclerosis.

The information in this Current Report on Form 8-K under Items 2.02 and 7.01, including the information contained in Exhibits 99.1 and 99.2, is being furnished to the Securities and Exchange Commission, and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934 or otherwise subject to the liabilities of that section, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934, except as shall be expressly set forth by a specific reference in such filing.

Item 8.01. Other Events.

On November 9, 2020, the Company presented additional data from its RESOLVE-1 Phase 3 study of lenabasum for the treatment of systemic sclerosis, as summarized below:

Modified intent-to-treat population (n = 363):

- Stable doses of background immunosuppressant therapies were allowed in both lenabasum and placebo arms, reflecting current clinical practice.
- 84% of RESOLVE-1 subjects were on background immunosuppressant therapies.
- As previously reported, median American College of Rheumatology Combined Response Index for Systemic Sclerosis (ACR CRISS) scores at Week 52 were 0.888 versus 0.887, for lenabasum 20 mg twice daily (n = 120) versus placebo (n = 123).

Placebo group (n = 123):

- Unprecedented improvement was seen in the placebo group in subjects who were concurrently receiving stable doses of background immunosuppressant therapies, especially subjects in their first two years on these therapies.
- Subjects treated with background mycophenolate had the greatest improvement over the one-year RESOLVE-1 study.

Post-hoc analyses of lenabasum 20 mg twice daily group compared to placebo group:

- In subjects receiving established background immunosuppressant therapies (> 2 years duration at baseline), lenabasum treatment (n = 38) versus placebo (n = 26) was associated with reduced decline in forced vital capacity (FVC) at one year, measured in milliliters (-21 mL versus -170 mL, nominal P = 0.048) or percent predicted (-0.4% versus -4.6%, nominal P = 0.039).
- Data from these subjects were also categorized as follows: FVC % decline (worsening by more than -5%), stable FVC % (values within 5% of baseline value) and improved FVC % (improvement more than 5%). Lenabasum 20 mg twice daily was associated with a lower likelihood of a decline (19% lenabasum versus 50% placebo), greater likelihood to have stable FVC % predicted (64% lenabasum versus 35% placebo), and similar likelihood in improvement (17% lenabasum versus 15% placebo, nominal P = 0.035).
- In a subset of these subjects with diagnosed interstitial/restrictive lung disease (ILD), lenabasum 20 mg twice daily was associated with numerically reduced decline in FVC at one year (-14 mL versus -121 mL and -0.3% versus -3.5%), lenabasum (n = 32) versus placebo (n = 20). ILD was identified by fibrosis on chest x-ray or computerized tomography of the lungs or baseline FVC < 80% predicted.

Safety findings:

- Lenabasum was safely administered and well tolerated in this study, with no new safety findings. Dizziness (18.3% lenabasum versus 4.9% placebo) and dry mouth (5.0% lenabasum versus 1.6% placebo) were among adverse events that occurred in ≥ 3% more subjects in the lenabasum 20 mg twice daily group versus the placebo group. No evidence of lenabasum-associated immunosuppression was seen.

Item 9.01. Financial Statements and Exhibits.

(d) The following exhibits are furnished with this report:

Exhibit No.	Description
99.1	Press Release issued by Corbus Pharmaceuticals Holdings, Inc. dated November 10, 2020.
99.2	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: November 10, 2020

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

Exhibit 99.1

Corbus Pharmaceuticals Reports Third Quarter Financial Results and Provides Corporate Updates

- *Company intends to shorten fully-enrolled Phase 3 dermatomyositis trial to 28 weeks from 52 weeks following recent developments in competitive landscape; data now expected as early as the second quarter of 2021*
- *Expected cash runway extended into second quarter of 2022 as a result of Company restructuring, with potential to extend cash runway even further due to shortening of Phase 3 dermatomyositis trial*
- *Company will also focus on progressing pipeline compounds toward clinical testing*
- *Reported topline data from RESOLVE-1 Phase 3 study of lenabasum in systemic sclerosis and data from Phase 2b study of lenabasum in cystic fibrosis; Corbus is exploring potential next steps in both indications*
- *Company to host conference call and webcast today, Tuesday, November 10, 2020 at 8:30 a.m. ET*

Norwood, MA, November 10, 2020 (GLOBE NEWSWIRE) — Corbus Pharmaceuticals Holdings, Inc. (NASDAQ: CRBP) ("Corbus" or the "Company"), a clinical-stage drug development company pioneering transformative medicines that target the endocannabinoid system ("ECS"), today reported financial results for the third quarter of 2020. The Company also provided clinical, pipeline and corporate updates.

Yuval Cohen, Ph.D., Chief Executive Officer said, "We are emerging from a very challenging period with a continued focus on our lenabasum dermatomyositis program and preclinical pipeline. Our restructuring significantly improved our cash runway, so we can continue to work toward delivering a much-needed novel therapeutic option for patients while also giving us the resources to look at external assets that will be synergistic to our in-house capabilities. We expect our cash runway to be further extended with the cost savings from our plan to shorten the **D**ETER**MI**NE Phase 3 dermatomyositis study to 28 weeks from one year. This decision is driven by recent changes in the dermatomyositis competitive landscape and will accelerate topline data readout to the second quarter of 2021. We see our dermatomyositis program as a potential large value driver for our Company, given that there are about 40,000 dermatomyositis patients in North America and limitations with current treatment options."

Dr. Cohen continued, "While we were disappointed that both the RESOLVE-1 systemic sclerosis study and the Phase 2b cystic fibrosis study did not meet their primary endpoints, we have a solid understanding of what led to those outcomes. The data generated point to clinical activity associated with lenabasum treatment. The dataset also provided unique insight into disease progression and the impact of current standards of care. With this in mind, we are working with systemic sclerosis and cystic fibrosis experts to further analyze the data and potentially explore paths forward in these programs."

Clinical Program Updates:

Lenabasum: a novel, oral, selective cannabinoid receptor type 2 (CB2) agonist

Dermatomyositis – The Phase 3 "**D**ETER**M**INE" study in dermatomyositis, a rare and life-threatening autoimmune disease characterized by skin and muscle inflammation, is fully enrolled.

Key Updates:

- This double-blind, randomized, placebo-controlled, multinational study enrolled 176 patients, which exceeded the original target of 150 patients. Approximately 60% of patients have completed Week 28 of dosing.
- There have been recent changes in the dermatomyositis competitive landscape with studies that are shorter than one year using the same efficacy endpoint as **D**ETER**M**INE. Therefore, Corbus will submit a protocol amendment to the FDA and other regulatory agencies to shorten the treatment duration of **D**ETER**M**INE to 28 weeks from one year. The last subject visit through 28 weeks is expected in March 2021 with topline data to be reported shortly thereafter.
- Baseline patient demographics and disease characteristics were presented at the American College of Rheumatology's (ACR) Convergence 2020, which took place November 5–9, 2020. ACR poster is available online.
- A separate presentation at ACR Convergence 2020 showed that CB2 expression was increased on immune cells in lesional skin from dermatomyositis subjects in the lenabasum Phase 2 study. Treatment with lenabasum was associated with reduction in immune cell infiltrates, CB2 expression and inflammatory cytokine production in lesional skin from these subjects. ACR poster is available online.
- There is significant unmet need for new medicines to achieve disease control in dermatomyositis because of the limitations of current treatment options. Dermatomyositis affects approximately 80,000 people in North America, EU and Japan.

- *Systemic Sclerosis* – Topline data from the RESOLVE-1 Phase 3 study of lenabasum for the treatment of systemic sclerosis were announced on September 8, and additional data were announced on November 9. RESOLVE-1 was a 52-week, multinational, double-blind, placebo-controlled study that enrolled 365 patients with diffuse cutaneous systemic sclerosis. It was the first large, late-stage clinical study in diffuse cutaneous systemic sclerosis that allowed patients to remain on a wide range of background immunosuppressive therapy.

Key Findings:

- Topline data remain as previously reported.
- Exploratory post-hoc analyses showed lenabasum treatment was associated with a benefit in lung function (forced vital capacity) in subjects on established background immunosuppressant therapies (greater than 2 years)
- Focusing on FVC in patients on established immunosuppressant therapies could address a key unmet need, which Corbus believes represent a potential commercial opportunity.
- Systemic sclerosis is a rare, life-threatening autoimmune disease affecting up to 75K Americans.

Next Steps:

- The Company is continuing to analyze the data and will consider the potential for an additional study based on results of these analyses.

- *Cystic Fibrosis* – Topline data from the CF-002 Phase 2b study of lenabasum for treatment of CF were announced on October 6 and presented at the North American Cystic Fibrosis Conference (NACFC) in October (NACFC Poster #817 available here). CF-002 was a 28-week multinational, double-blind, randomized, placebo-controlled study that dosed 426 subjects who were at high-risk for recurrent pulmonary exacerbations (PEx). It is the first study to enroll subjects who are prone to exacerbation despite being on standard of care, including CFTR modulators.

Key Findings:

- Topline data remain as previously reported.
- Lenabasum did not meet its primary efficacy endpoint in the study.
- Lenabasum was well tolerated with no new safety findings.
- Exploratory post-hoc analyses revealed unexpectedly low PEx rates in subjects from five eastern European countries (21% of total subjects) who received placebo. Pulmonary exacerbations rates in these subjects were 85% lower than in subjects from other countries.
- Exploratory post-hoc analyses in subjects with similar FEV1% predicted at baseline and similar treatment with CFTR-modulators suggested evidence of clinical benefit of lenabasum.
- PEx remains a significant burden in people with CF even with current standard therapies, including antibiotics and CFTR modulators.

Next Steps:

- Further analysis of the data is underway to determine potential next steps.

- *Systemic Lupus Erythematosus (SLE)* – The Phase 2b study is ongoing. The study, funded and managed by the National Institutes of Health (NIH), is enrolling at 15 sites in the U.S., with enrollment expected to be completed in the first half of 2021.

Pipeline Updates:

- Corbus has identified several compounds from its CB1 inverse agonist program which the Company believes has more promising physicochemical and pharmacokinetic properties than CRB-4001. The Company is shifting its focus to prioritize development of these compounds and not continuing with CRB-4001. The Company is also looking for attractive external assets that could have a strong synergy with is organizational capabilities, pipeline and expertise in immunology. Corbus will provide an update at its next R&D day.

Corporate Updates:

- On October 8, Corbus announced a reduction in workforce and restructuring of its operations designed to reduce costs and reallocate resources towards its lenabasum clinical development program in dermatomyositis and systemic lupus erythematosus, as well as the Company's pipeline of other novel ECS-targeting drug candidates. The restructuring, which included cost reductions, was intended to extend the Company's cash runway, and, together with the shortening of the DM study to 28 weeks, is designed to extend the Company's cash runaway beyond the second quarter of 2022.

Financial Results for Third Quarter Ended September 30, 2020:

For the quarter ended September 30, 2020, the Company reported a net loss of approximately $34.9 million or a net loss per diluted share of $0.43, compared to a net loss of approximately $20.8 million or net loss per diluted share of $0.32 for the quarter ended September 30, 2019.

For the quarter ended September 30, 2020 revenue decreased by approximately $1.4 million from the third quarter of 2019 to $1.2 million, due primarily to revenue recognized under the Cystic Fibrosis Program Related Investment Agreement.

Operating expenses for the quarter ended September 30, 2020 increased by approximately $7.5 million to $35.2 million. The increase was primarily attributable to increased clinical trial costs.

Corbus expects its cash and cash equivalents on hand of approximately $81.9 million at September 30, 2020 together with proceeds from the expected final $2.5 million milestone payment from the Cystic Fibrosis Foundation and anticipated foreign tax credits, to fund operations and its current clinical plan beyond the second quarter of 2022.

Conference Call and Webcast Information:

Corbus management will host a conference call and webcast presentation for investors, analysts, and other interested parties today, Tuesday, November 10, 2020, at 8:30 a.m. ET.

To participate on the call, please dial (877) 407-3978 (domestic) or (412) 902-0039 (international). The live webcast will be accessible on the Events page of the Investors section of the Corbus website, www.corbuspharma.com, and will be archived for 90 days.

About Corbus

Corbus Pharmaceuticals Holdings, Inc. is a clinical-stage company focused on the development and commercialization of novel medicines designed to target the endocannabinoid system. The Company's lead product candidate, lenabasum, is a novel, oral, selective cannabinoid receptor type 2 (CB2) agonist designed to provide an alternative to immunosuppressive medications in the treatment of chronic inflammatory and fibrotic diseases. Lenabasum is currently being evaluated in dermatomyositis and systemic lupus erythematosus. Corbus is also developing a pipeline of other preclinical drug candidates from its endocannabinoid system platform.

Lenabasum is not approved for the treatment of any indication. For more information on Corbus' clinical programs, please visit here.

For more information, visit http://www.corbuspharma.com/, and connect with us on Twitter, LinkedIn, and Facebook.

Forward-Looking Statements

This press release 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.

Corbus Pharmaceuticals Holdings, Inc.
Condensed Consolidated Balance Sheets

	September 30, 2020 (unaudited)	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 81,870,651	$ 31,748,686
Restricted cash	350,000	—
Prepaid expenses and other current assets	2,177,383	3,724,932
Contract asset	960,091	2,681,065
Total current assets	85,358,125	38,154,683
Restricted cash	669,900	—
Property and equipment, net	4,402,022	5,083,865
Operating lease right of use asset	5,396,248	5,818,983
Other assets	13,041	84,968
Total assets	$ 95,839,336	$ 49,142,499
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Notes payable	$ —	$ 752,659
Accounts payable	11,080,717	11,091,363
Accrued expenses	28,593,049	22,447,939
Derivative liability	757,000	—
Operating lease liabilities, current	972,464	595,745
Total current liabilities	41,403,230	34,887,706
Long-term debt, net of debt discount	17,856,589	—
Operating lease liabilities, noncurrent	7,353,765	8,097,228
Total liabilities	$ 66,613,584	$ 42,984,934
Stockholders' equity		
Preferred Stock $0.0001 par value:10,000,000 shares authorized, no shares issued and outstanding at September 30, 2020 and December 31, 2019	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized, 82,207,405 and 64,672,893 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	8,220	6,467
Additional paid-in capital	324,698,962	198,975,056
Accumulated deficit	(295,481,430)	(192,823,958)
Total stockholders' equity	29,225,752	6,157,565
Total liabilities and stockholders' equity	$ 95,839,336	$ 49,142,499

Corbus Pharmaceuticals Holdings, Inc.
Consolidated Statements of Operations
(Unaudited)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2020	**2019**	**2020**	**2019**
Revenue from awards and licenses	$ 1,230,621	$ 2,589,783	$ 3,279,026	$ 33,570,048
Operating expenses:				
Research and development	27,522,989	22,152,001	82,156,926	66,117,114
General and administrative	7,681,573	5,534,493	23,120,020	17,367,202
Total operating expenses	35,204,562	27,686,494	105,276,946	83,484,316
Operating loss	(33,973,941)	(25,096,711)	(101,997,920)	(49,914,268)
Other income (expense), net:				
Other income (expense), net	(4,972)	4,109,338	4,005	4,109,338
Interest income (expense), net	(454,319)	292,854	(348,654)	1,076,166
Change in fair value of derivative liability	(211,000)	-	(211,000)	-
Foreign currency exchange loss, net	(251,117)	(96,282)	(103,903)	(144,193)
Other income (expense), net	(921,408)	4,305,910	(659,552)	5,041,311
Net loss	$ (34,895,349)	$ (20,790,801)	$ (102,657,472)	$ (44,872,957)
Net loss per share, basic and diluted	$ (0.43)	$ (0.32)	$ (1.37)	$ (0.71)
Weighted average number of common shares outstanding, basic and diluted	81,879,119	64,660,017	75,037,418	63,638,447

Corbus Pharmaceuticals Contacts:

Ted Jenkins, Senior Director, Investor Relations and Corporate Communications
Phone: +1 (617) 415-7745
Email: ir@corbuspharma.com

Lindsey Smith, Director, Investor Relations and Corporate Communications
Phone: +1 (617) 415-7749
Email: mediainfo@corbuspharma.com

Exhibit 99.2

CORBUS PHARMACEUTICALS™

Pioneering transformative medicines that target the endocannabinoid system

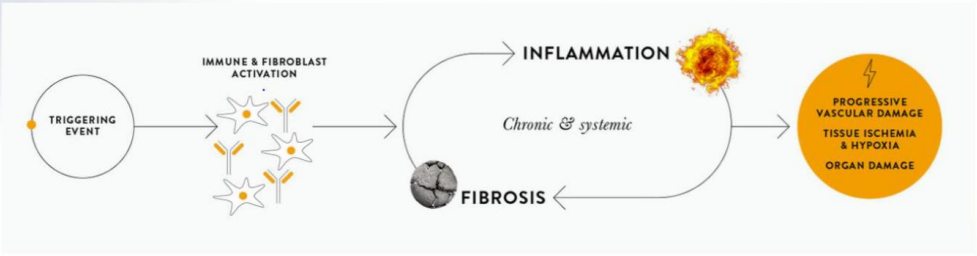
RESOLVE-1 Phase 3 Study of Lenabasum in Systemic Sclerosis

@corbuspharma

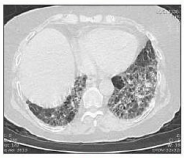
NASDAQ: CRBP
www.corbuspharma.com

Systemic Sclerosis: The Unmet Need

Systemic sclerosis is a rare, debilitating and life-threatening autoimmune disease characterized by inflammation & fibrosis



~200,000
people with SSc in US, EU and Japan[1]

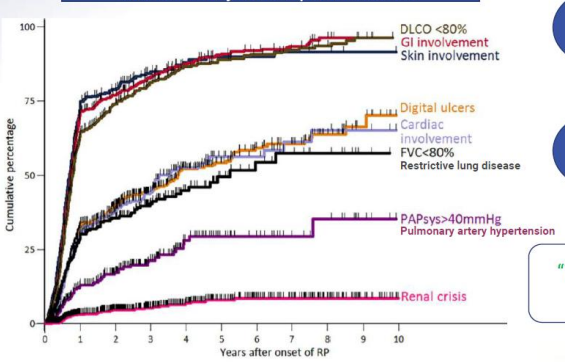


Interstitial Lung Disease in SSc

Patient Images (bottom) Provided by the Scleroderma Foundation;

Systemic sclerosis has among the highest mortality of systemic autoimmune diseases, driven primarily by its deleterious effects on major organs

Incident organ involvement in SSc from onset of Raynaud's phenomenon



Source: Jaeger VK, et al. PLoS One 2016. doi:10.1371/journal.pone.0163894.g003
Abbreviations: RP, Raynaud's Phenomenon; DLCO, single breath diffusing capacity for monoxide; FVC, forced vital capacity; PAPsys, systolic pulmonary artery pressure as estimated by echocardiography

4 x Patients with SSc have four times (4x) greater risk of death than their healthy counterparts

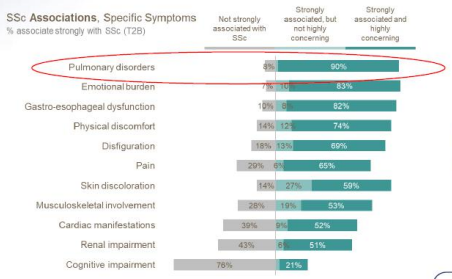
~11 years Median 11 years of survival

"Treatment for scleroderma is the number one unmet need in rheumatology today."

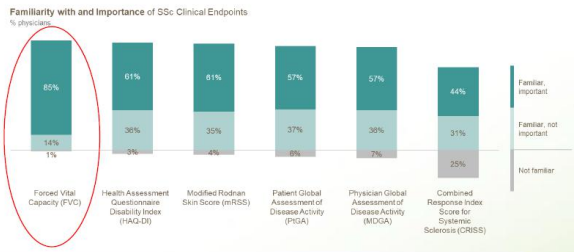
US Treatment Center Rheumatologist

Physicians are most concerned with lung involvement in SSc

Rheumatologists rank pulmonary disorders as the most strongly associated and highly concerning of SSc specific symptoms…



...they are also most familiar with, and find most important, forced vital capacity (FVC) as an SSc endpoint



"How severe is the organ-system involvement, that is the crucial issue, GI and lung. Lung is the biggest concern."

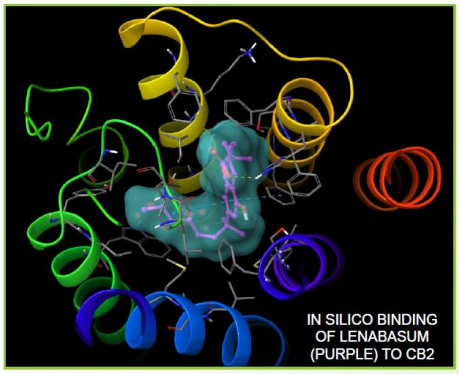
US Community Rheumatologist

Source: Corbus SSc ATU Study, March 2020 (n = 100 US Rheumatologists)

Rationale for Lenabasum in Systemic Sclerosis

Lenabasum is a CB2 agonist designed to provide an alternative to immunosuppressive treatments for chronic inflammatory and fibrotic diseases

- Oral agonist of cannabinoid receptor type 2 (CB2), a GPCR that regulates inflammation and fibrosis
- Designed as a disease-modifying **alternative to immunosuppressive treatments** for chronic inflammatory and fibrotic diseases
- Has effects on immune cells and fibroblasts, both of which express CB2 when activated
- Reduces inflammatory cells and cytokines in tissue
- Reduces myofibroblasts and pro-fibrotic growth factors in tissue



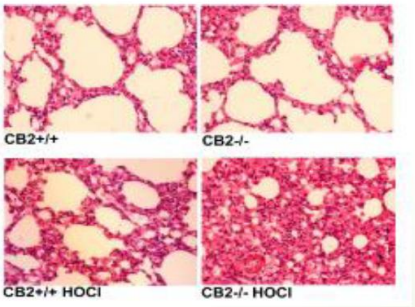
Animal model data provide link between CB2 and systemic sclerosis

Mice without CB2 (CB2-/- knock-out mice) develop excessive **lung and skin fibrosis** and **SSc-specific autoantibodies** (anti-DNA topoisomerase 1 antibodies) when their immune system is activated with hypochlorite (HOCl)[1].

Lung fibrosis is shown.

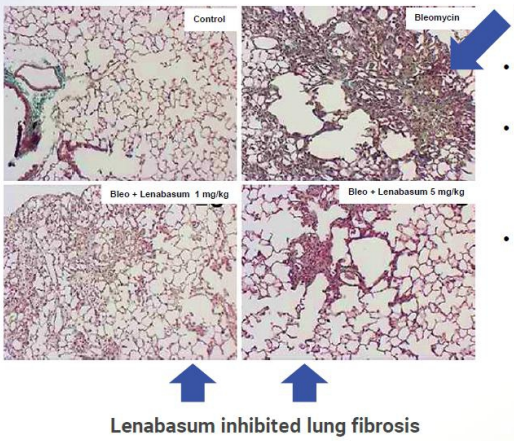
Servettaz et al. Am J Pathol 2010;177:187-96

Excessive lung fibrosis develops in mice without CB2



Excessive lung fibrosis in absence of CB2

Lenabasum reduced fibrosis in an animal model of SSc lung disease



Lenabasum inhibited lung fibrosis

Lung fibrosis induced with bleomycin

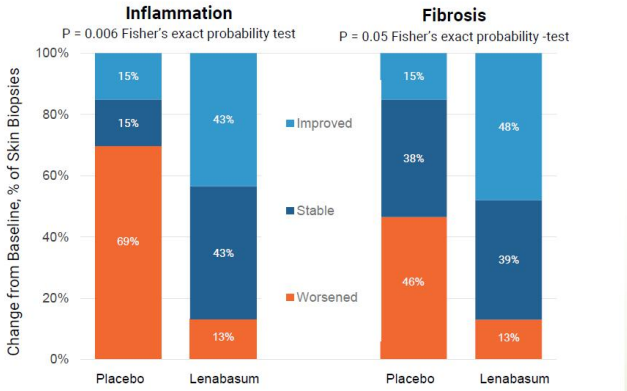
- Lung fibrosis is induced with bleomycin (bleomycin versus control)
- Lenabasum, whether started prophylactically before bleomycin or therapeutically 1 week after bleomycin, reduced lung inflammation and fibrosis
- Lung histology is shown for Day 14 post-bleomycin, when lenabasum was starting therapeutically at Day 8

Lucatelli, Respir Res. 2016;17:49

Phase 2 Biomarkers

Phase 2 | Lenabasum improved inflammation and fibrosis in skin biopsies from SSc patients in a Phase 2 study

More improvement or stability of histological findings of inflammation and fibrosis in paired skin biopsies after 12 weeks treatment with lenabasum versus placebo



Analyses are of paired skin biopsies at baseline and Week 12, N = 23 lenabasum and N = 13 placebo.

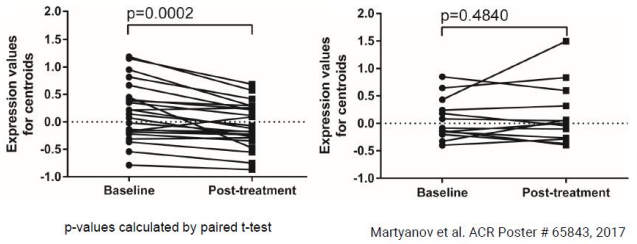
Phase 2 Biomarkers

Phase 2 | Lenabasum reduced expression of gene pathways involved in fibrosis in skin biopsies from SSc patients

Greater reduction in gene ontology pathways associated with inflammation and fibrosis in paired skin biopsies after 12 weeks treatment with lenabasum versus placebo.

Results are shown for the extracellular matrix organization gene ontology pathway

Extracellular Matrix Organization Pathway



p-values calculated by paired t-test

Martyanov et al. ACR Poster # 65843, 2017

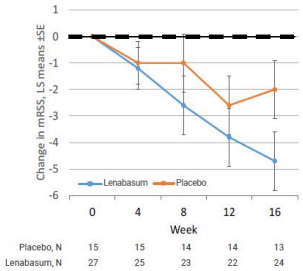
Analyses are of paired skin biopsies at baseline and Week 12, N = 23 lenabasum and N = 13 placebo.

Phase 2 Efficacy

Phase 2 | Lenabasum improved efficacy results in a 16-week Phase 2 study in SSc

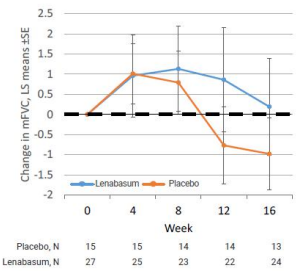
Greater numerical reduction in modified Rodnan skin score (mRSS), a measure of skin fibrosis, and forced vital capacity (FVC) percent predicted, a measure of lung function, after 12 weeks treatment with lenabasum versus placebo

Change in mRSS



Placebo, N	15	15	14	14	13
Lenabasum, N	27	25	23	22	24

Change in FVC, % predicted



Placebo, N	15	15	14	14	13
Lenabasum, N	27	25	23	22	24

RESOLVE-1 Phase 3 Study Design and Results

Phase 3 | Eligibility criteria and efficacy endpoints in the RESOLVE-1 Phase 3 study were similar to those in Phase 2

Phase 3 Design

- Double-blind, randomized, placebo-controlled, 52-week study of lenabasum in diffuse cutaneous SSc
- ACR CRISS at Week 52 was the primary efficacy endpoint
- Change in FVC % predicted was a secondary efficacy endpoint

Design

Primary endpoint: ACR-CRISS

365 subjects

52 weeks

76 sites in

1:1:1 dosing — 20 mg BID | 5 mg BID | Placebo

SECONDARY ENDPOINTS

- Change from baseline in mRSS
- Change from baseline in HAQ-DI
- Change from baseline in FVC % predicted

Orphan Drug Designation from FDA, EMA and PMDA
Fast Track status from FDA

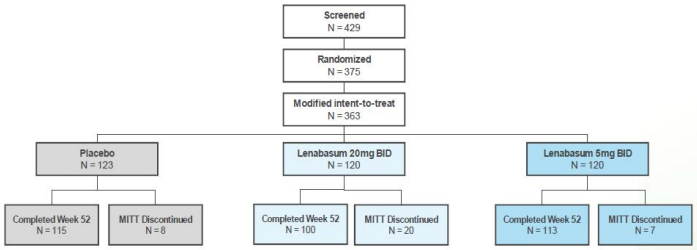
Eligibility

- Diffuse cutaneous SSc
- Disease duration ≤ 6 years. If 3-6 years, then mRSS ≥ 15
- Most background immunosuppressive therapies allowed if:
  - Stable for at least 8 weeks before Screening
  - Steroids not to exceed 10 mg prednisone per day or equivalent
- Decision to allow background immunosuppressive therapies was made to reflect current clinical practice

Phase 3 Disposition

Phase 3 | 90% of the modified intent-to-treat population completed the RESOLVE-1 Phase 3 study

Lower than anticipated drop-out rate of 9.6%



Modified intent-to-treat (mITT) population included subjects who received at least 1 dose of study drug and had at least 1 efficacy assessment after baseline.

Phase 3 | Baseline demographics in RESOLVE-1 were as expected

Phase 3 Baseline

- Many subjects were middle-aged, white, non-Hispanic females
- About 37% of subjects were from the United States

	Placebo N = 123	Lenabasum 5 mg N = 120	Lenabasum 20 mg N = 120
Age, years, mean (SD)	51.9 (12.38)	49.7 (13.51)	49.7 (12.87)
Female, %	74.0	73.3	80.0
Race, %			
White	71.5	66.7	70.0
Asian	21.1	20.0	20.0
Black	3.3	6.7	5.0
Hispanic, %	8.1	5.0	11.7
BMI (kg/m^2) (SD)	24.8 (5.27)	24.5 (4.96)	25.0 (5.61)
US, %	37.4	37.5	36.7
Canada/Europe/Israel/Australia, %	44.7	45.8	45.0
Asia (Japan and South Korea), %	17.9	16.7	18.3

Phase 3 | Baseline disease characteristics in RESOLVE-1 were as expected

Phase 3 Baseline

Subjects had moderate to severe disease despite frequent treatment with immunosuppressants

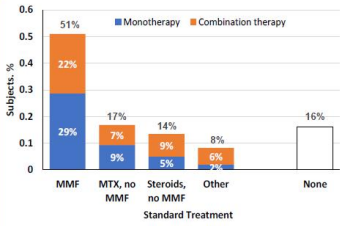
Characteristic (range)	Placebo N = 123	Lenabasum 5 mg N = 120	Lenabasum 20 mg N = 120
	N (%) or mean (SD)		
Disease duration, months	30.2 (16.84)	32.2 (17.62)	32.7 (19.94)
<= 3 years	66%	59%	61%
> 3 years	34%	41%	39%
Modified Rodnan Skin Score (0-51)	23.3 (8.68)	22.0 (7.35)	22.1 (8.55)
Physician Global Assessment (0-10)	5.6 (1.71)	5.4 (1.58)	5.3 (1.46)
Health Assessment Questionnaire (0-3)	1.16 (0.768)	1.07 (0.765)	1.12 (0.782)
Patient Global Assessment (0-10)	5.0 (2.10)	4.8 (2.16)	5.0 (2.10)
Forced Vital Capacity, % predicted	78.9 (15.23)	79.5 (16.13)	81.3 (18.8)
Immunosuppressive Use	84%	78%	89%

Phase 3 Background Meds

Phase 3 | The majority of subjects in RESOLVE-1 were receiving background treatment with the immunosuppressant mycophenolate

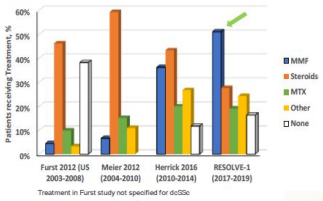
- 84% of RESOLVE-1 subjects were receiving stable doses of background immunosuppressive therapies (IST)
- Mycophenolate was the dominant IST
- Use of mycophenolate appears to be increasing in clinical practice

Background immunosuppressive therapy use in RESOLVE-1



- Only 16% were not receiving with background immunosuppressive therapies (IST)
- About half (51%) of subjects in RESOLVE-1 were on background mycophenolate

Increasing use of mycophenolate



Treatment in Furst study not specified for dcSSc

With time

- Fewer patients not receiving any IST
- **MMF may be becoming the dominant IST**
- Less steroid use

Phase 3 | Baseline immunosuppressant therapies appeared to influence efficacy outcomes in RESOLVE-1

Phase 3 IST

- Efficacy was much higher than expected in the placebo group
- Background IST appeared to cause the high efficacy in the placebo group, especially mycophenolate and other IST started within 2 years before baseline

Placebo group, Week 52

	N	ACR CRISS, median	Change in mRSS, mean	Change in FVC%, mean	Change in FVC, mL, mean
All placebo subjects[1]	113	0.894	-8.0	-1.2	-51
Any immunosuppressant therapy (IST)	97	0.936	-8.9	-1.0	-43
No IST	16	0.417	-2.3	-2.8	-97
Mycophenolate (MMF) ± any other IST	62	0.953	-10.1	0.1	-8
No MMF, any other IST	35	0.747	-6.8	-2.9	-107
MMF started ≤ 2 years before baseline	47	0.994	-11.6	1.3	31
MMF started > 2 years before baseline	15	0.652	-5.5	-3.6	-130
All non-MMF IST started ≤ 2 years before baseline, no MMF	24	0.931	-6.7	-1.4	-52
≥ 1 non-MMF IST started > 2 years before baseline, no MMF	11	0.301	-6.9	-6.1	-225
All IST started ≤ 2 years before baseline	71	0.962	-10.0	0.4	3
≥ 1 background IST started > 2 years before baseline; MMF must be > 2 years duration (established IST)	26	0.619	-6.1	-4.6	-170

- Higher ACR CRISS score is greater improvement
- Negative change in mRSS is improvement, positive change is worsening
- Positive change in FVC % predicted or mL is improvement, negative change is worsening

Per protocol population, completed study and study drug, LOCF for missing mRSS, FVC values

Phase 3 | There were no significant differences among treatment groups in primary efficacy outcome, ACR CRISS score, at Week 52

Phase 3 ACR CRISS

- ACR CRISS score was much higher than expected in the placebo group
- No additional efficacy discerned in lenabasum cohorts

	Lenabasum 20 mg BID N = 120	Lenabasum 5 mg BID N = 120	Placebo N = 123
Visit 11 (Week 52)			
n	100	113	115
Mean (SD)	0.5983 (0.43229)	0.5749 (0.42319)	0.6360 (0.42229)
Median (Q1, Q3)	0.8880 (0.0610, 0.9970)	0.8270 (0.0700, 0.9880)	0.8870 (0.0710, 0.9990)
p-value - Ranked Score, MMRM	0.4972	0.3486	

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. Table 14.2.1.1

Phase 3 ACR CRISS

Phase 3 | Few subjects in RESOLVE-1 had ACR CRISS Step 1 = 0 scores that indicate very bad heart, lung, or renal outcomes

Low numbers of subjects in RESOLVE-1 experienced very bad heart, lung, or renal outcomes, as measured using ACR CRISS Step 1 criteria

ACR CRISS Step 1 = 0 score indicates subject developed new significant, heart, lung, or kidney involvement, using pre-specified criteria

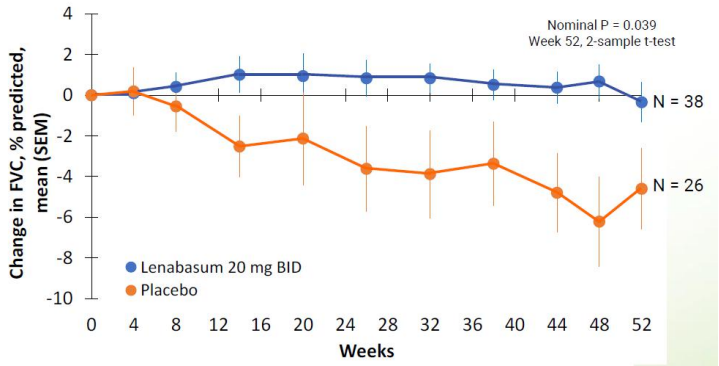
Step 1 Criteria	Placebo N = 123, n (%)	Lenabasum 5 mg BID N = 120, n (%)	Lenabasum 20 mg BID N = 120, n (%)
New renal crisis, hypertensive	1	-	-
New pulmonary artery hypertension	-	-	-
New congestive heart failure	-	1	1
New interstitial lung disease (ILD)	3	3	1
New ILD at ≥ 2 consecutive visits	3	1	-
Total	4 (3.3%)	4 (3.4%)	2 (1.7%)

Detailed criteria can be found in Khanna. Arthritis Rheumatol. 201;68:299-311

Phase 3 Efficacy

Phase 3 | Subjects treated with lenabasum 20 mg BID added to established IST (> 2 years duration) had stable **FVC % predicted**

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



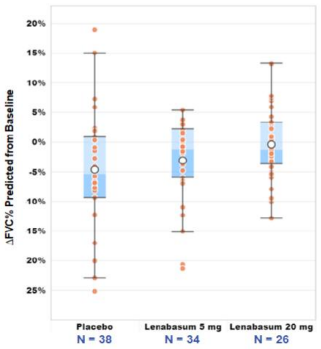
IST = immunosuppressant therapies. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and any MMF treatment must be > 2 years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

Phase 3 Efficacy

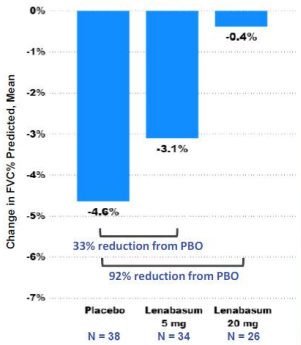
Phase 3 | Subjects treated with lenabasum 20 mg BID added to established IST had stable **FVC % predicted** over 1 year

Subjects had more stable lung function (FVC, % predicted) over 1 year when lenabasum 20 mg BID was added to established immunosuppressive therapies, compared to subjects treated with placebo

Change in FVC% predicted individual values, Week 52



Change in mean FVC% predicted, Week 52

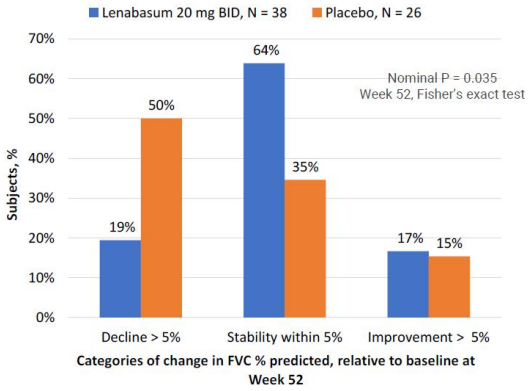


IST = immunosuppressant therapies. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and any MMF treatment must be > 2 years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

Phase 3 Efficacy

Phase 3 | Subjects treated with lenabasum 20 mg BID added to established IST had less decline and more stability in **FVC % predicted**

A lower proportion of subjects treated with lenabasum 20 mg BID added to established immunosuppressive therapies had worsening lung function and a higher proportion had stable lung function, compared to subjects treated with placebo

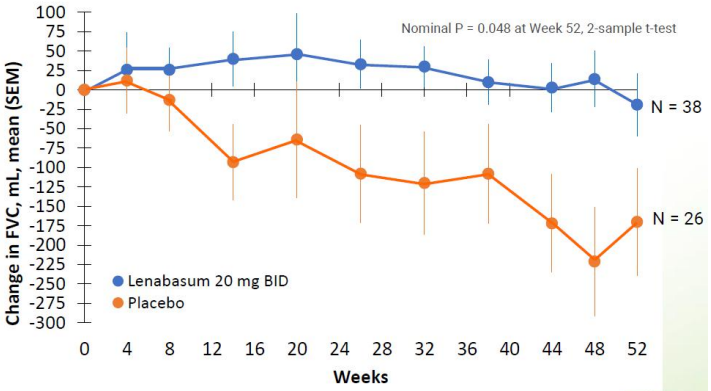


IST = immunosuppressant therapies. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and any MMF treatment must be > 2 years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

Phase 3 Efficacy

Phase 3 | Subjects treated with lenabasum 20 mg BID added to established IST had stable **FVC mL** over 1 year

Subjects treated with lenabasum 20 mg BID added to established immunosuppressive therapies had stable FVC, mL over 1 year



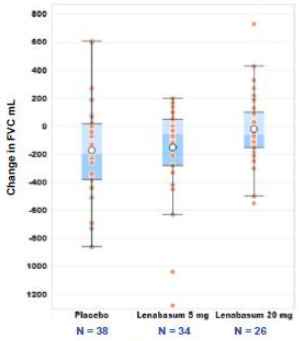
IST = immunosuppressant therapies. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and any MMF treatment must be > 2 years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

Phase 3 Efficacy

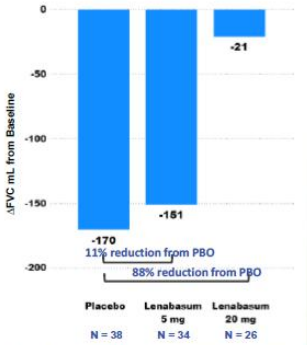
Phase 3 | Subjects treated with lenabasum 20 mg BID added to established IST had stable **FVC % predicted** over 1 year

Subjects had more stable lung function (FVC, mL) over 1 year when lenabasum 20 mg BID, rather than placebo, was added to established immunosuppressive therapies

Change in FVC% predicted individual values, Week 52



Change in mean FVC% predicted, Week 52



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

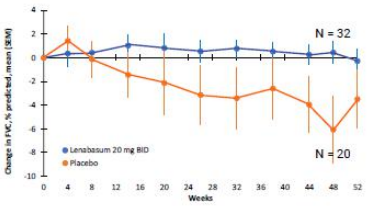
Phase 3 Efficacy

Phase 3 | **Subjects with ILD** treated with lenabasum 20 mg BID added to established IST also had stable **FVC mL** over 1 year

Subjects with interstitial lung disease treated with lenabasum 20 mg BID added to established immunosuppressive therapies had stable FVC, % predicted over 1 year

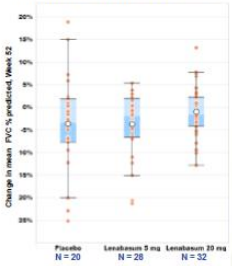
Interstitial lung disease (ILD) was defined as history of fibrosis on chest X-ray or computerized tomography of lungs or pattern of restrictive lung disease on spirometry including FVC < 80% predicted at baseline

Change in FVC mL over 1 year



Not statistically significant, Week 52

Change in FVC mL individual values, Week 52

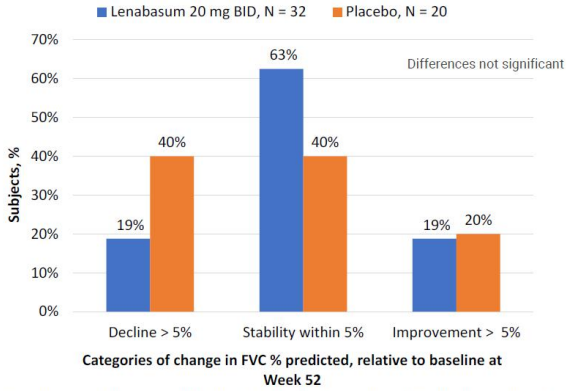


IST = immunosuppressant therapies. ILD = interstitial lung disease. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline, and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

Phase 3 | **Subjects with ILD** treated with lenabasum 20 MG BID added to established IST had less worsening and more stability in **FVC % predicted**

Phase 3 Efficacy

Numerically lower proportions of subjects treated with lenabasum added to established IST had worsening lung function and a higher proportion had stable lung function, compared to subjects treated with placebo



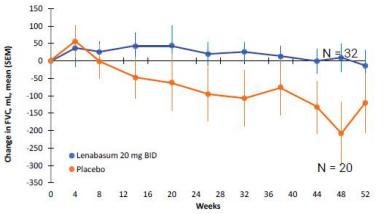
IST = immunosuppressant therapies. ILD defined as described in previous slide. Post-hoc analyses, per protocol population of subjects who completed study drug and Week 52, LOCF for any missing values. Subjects were receiving at least 1 background IST for greater than 2 years treatment duration at baseline,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

Phase 3 | **Subjects with ILD** treated with lenabasum 20 mg BID added to established IST also had stable **FVC mL** over 1 year

Phase 3 Efficacy

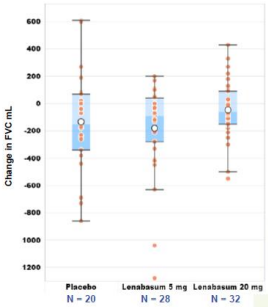
Subjects with interstitial lung disease treated with lenabasum 20 mg BID added to established immunosuppressive therapies had stable FVC, mL over 1 year

Change in FVC mL over 1 year



Not statistically significant, Week 52

Change in FVC mL individual values, Week 52



IST = immunosuppressant therapies. ILD defined as described in previous slide. 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.

Phase 3 Safety

Phase 3 | Lenabasum's safety profile remained favorable in RESOLVE-1

Lenabasum's safety profile was favorable, with fewer serious and severe AEs in lenabasum groups compared to placebo

Lenabasum was well-tolerated with no potentially or definitely-related TEAE leading to study drug discontinuation

Treatment-emergent Adverse Events (TEAE)	Placebo N = 123, n (%)	Lenabasum 5 mg N = 120, n (%)	Lenabasum 20 mg N = 120, n (%)
Any TEAE	106 (86.2)	110 (90.2)	110 (91.7)
Any Serious TEAE	18 (14.6)	10 (8.2)	11 (9.2)
Any TEAE by Maximum Severity			
Mild	44 (35.8)	47 (38.5)	55 (45.8)
Moderate	46 (37.4)	59 (48.4)	48 (40.0)
Severe	16 (13.0)	4 (3.3)	7 (5.8)
Any TEAE by Strongest Relationship			
Unrelated	41 (33.3)	35 (28.7)	36 (30.0)
Unlikely	30 (24.4)	34 (27.9)	27 (22.5)
Possible	33 (26.8)	36 (29.5)	42 (35.0)
Probable	2 (1.6)	5 (4.1)	4 (3.3)
Definite	0	0	1 (0.8)
Any TEAE Leading to Study Drug Discontinuation	7 (5.7)	2 (1.6)	5 (4.2)
Potentially Related TEAEs Leading to Study Drug Discontinuation	1 (0.8)	0	0
Any TEAE Leading to Death	1 (0.8)	0	1 (0.8)

Safety population of 365 subjects receiving at least 1 dose of study drug. Deaths during active treatment were unrelated to study drug. Death in the placebo group was from rapidly progressing SSc with respiratory and renal failure. Death in the lenabasum 20 mg group was from myocarditis leading to heart and respiratory failure.

Phase 3 Safety

Phase 3 | TEAEs occurring in at least 3% more of lenabasum 20 mg twice daily or placebo group, compared to the other group

Likely class effects of dizziness, dry mouth and somnolence occurred more frequently in lenabasum groups than placebo

No increase in neutropenia, opportunistic infections, or malignancies was seen to suggest immunosuppression

At least 3% more frequent in lenabasum 20 mg twice daily than placebo groups

System Organ Class	Placebo N=123, n (%)	Lenabasum 5 mg BID N=122, n (%)	Lenabasum 20 mg BID N=120, n (%)
Dizziness	6 (4.9%)	11 (9.0%)	22 (18.3%)
Dry mouth	2 (1.6%)	7 (5.7%)	6 (5.0%)
Somnolence	0	1 (0.8%)	5 (4.2%)
Nausea	13 (10.6%)	5 (4.1%)	17 (14.2%)
Vomiting	7 (5.7%)	7 (5.7%)	15 (12.5%)
UTI	6 (4.9%)	10 (8.2%)	13 (10.8)
Hematuria	0	4 (3.3%)	6 (5.0%)
Nasopharyngitis	10 (8.1%)	25 (20.5%)	18 (15.0%)
Headache	9 (7.3%)	14 (11.5%)	17 (14.2%)
Somnolence	0	1 (0.8%)	5 (4.2%)

At least 3% more frequent in placebo than lenabasum 20 mg twice daily groups

System Organ Class	Placebo N=123, n (%)	Lenabasum 5 mg BID N=122, n (%)	Lenabasum 20 mg BID N=120, n (%)
Anemia	7 (5.7%)	1 (0.8%)	2 (1.7%)
Arthralgia	20 (16.3)	15 (12.3%)	12 (10.0%)
Muscle weakness	4 (3.3%)	2 (1.6%)	0
Rotator cuff syndrome	4 (3.3%)	1 (0.8%)	0
Anxiety	5 (4.1%)	3 (2.5%)	1 (0.8%)
Productive cough	5 (4.1%)	0	0

Safety population of 365 subjects receiving at least 1 dose of study drug

Summary

Summary of RESOLVE-1 Phase 3 study results

- There were no significant differences between lenabasum 20 mg BID and placebo in the primary and secondary endpoints at Week 52
- Unprecedented improvement was observed in subjects in the placebo group. Improvement in the placebo group was greatest in subjects on background immunosuppressive therapies for ≤ 2 years treatment duration, especially mycophenolate
- Subjects treated with lenabasum 20 mg BID added to established immunosuppressive therapies had stable to little change in lung function assessed as FVC % predicted or FVC mL over 1 year, when compared to subjects treated with placebo
- Lenabasum was administered safely and was well-tolerated in this study, with no new safety signals or evidence of immunosuppression observed