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# Lenabasum for diffuse cutaneous systemic sclerosis

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## LAY SUMMARY

Systemic Sclerosis (SS) is a rare disease caused by the immune system attacking the tissue which lines underneath the skin and internal organs (connective tissue). The exact cause of SS is not known but it is thought to happen when immune cells attack the body's own tissues leading to the cells in the connective tissue producing too much collagen which causes scaring and thickening of the tissue. There are 2 types of SS; limited cutaneous SS (a milder form of SS affecting only parts of the body) and diffuse cutaneous SS (a more severe form of SS which can affect the whole body). The main symptoms of diffuse cutaneous SS are hardening of the skin, acid reflux, vomiting and diarrhoea, muscular pain, weakness and cramps. The outlook for people with diffuse cutaneous SS is generally poor due to high risk of life threatening complications such as heart, lung and kidney problems.

Lenabasum is being developed for diffuse cutaneous SS as a tablet to be taken twice per day. It works by binding to immune cells and triggers a process which reduces inflammation and the scaring and thickening of tissues which usually happens in SS. If licensed, lenabasum has the potential to reduce the scaring which happens in diffuse cutaneous SS and improve symptoms.



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## TARGET GROUP

Systemic sclerosis (diffuse cutaneous)

## TECHNOLOGY

## DESCRIPTION

Lenabasum (ajulemic acid; JBT101; CPL 7075; CT 3; IP 751; resunab; previously anabasum;) is a synthetic, oral, small-molecule, selective cannabinoid receptor type 2 (CB2) agonist that preferentially binds to CB2 expressed on activated immune cells and fibroblasts. CB2 activation triggers physiologic pathways that resolve inflammation, speed bacterial clearance and halt fibrosis. CB2 activation also induces the production of specialized pro-resolving lipid mediators that activate an endogenous cascade responsible for the resolution of inflammation and fibrosis, while reducing production of multiple inflammatory mediators. Through activation of CB2, lenabasum also is designed to have a direct effect on fibroblasts to halt tissue scarring.[1]

In the phase III clinical trial to evaluate efficacy and safety of lenabasum in diffuse cutaneous systemic sclerosis (RESOLVE-1: NCT03398837), lenabasum was administered orally at 5mg or 20mg twice daily for up to 1 year.[2]

Lenabasum does not currently have Marketing Authorisation in the EU for any indication.

Lenabasum is currently in phase II trials for cystic fibrosis, dermatomyositis and systemic lupus erythematosus.[2, 3, 4, 5]

## INNOVATION and/or ADVANTAGES

Through its novel mechanism of action, lenabasum has the potential to slow the progression of systemic sclerosis (SS) by resolving inflammation and reducing scaring and fibrosis. The treatment of fibrosis is an important unmet need in the treatment of SS as discussed by an EU Key Opinion Leader:

"I think probably we have to use anti-fibrotic drugs before fibrosis is actually occurring, and sometimes, even [if] we treat diffuse cutaneous scleroderma, even at an early stage, the six early months, sometimes it's too late. This is [what is] most challenging in scleroderma."
*(EU Key Opinion Leader – Global Data)*[6]

## DEVELOPER

Corbus Pharmaceuticals Inc.

## REGULATORY INFORMATION/ MARKETING PLANS

Lenabasum is a designated orphan drug in the EU and USA (December 2015) for systemic sclerosis.[7, 8]

Lenabasum was designated Fast Track status is the USA for systemic sclerosis.[9]

# PATIENT GROUP

## BACKGROUND

Systemic Sclerosis (SS) (or scleroderma) is a rare, chronic autoimmune disease where the immune system attacks the body's own tissues, in this case the connective tissues which underlie the skin and surround the organs and blood vessels.[10] This is thought to lead to the characteristic changes associated with SS, the excess synthesis and deposition of collagen in the skin and connective tissues.[11]

There are two main types of scleroderma; localised and systemic. Localised scleroderma affects just the skin and comes in two types; morphoea and linear. Systemic Scleroderma (SS) affects internal organs as well as skin and comes in two types; limited cutaneous SS and diffuse cutaneous SS (dcSS). Limited cutaneous SS is a milder form of SS which usually affects the skin on the hands, lower arms, feet, lower legs and face and eventually the lungs and digestive system. It often starts with Raynaud's syndrome (a circulation problem causing the hands and feet to turn white in the cold) and gradually gets worse over time. Diffuse SS is more likely to affect internal organs and skin changes can occur anywhere on the body. The main symptoms of diffuse SS include weight loss, fatigue, joint pain and stiffness and usually appear suddenly and worsen quickly over the first few years, after which symptoms may settle down. In some cases of diffuse SS, the heart, lungs or kidneys are affected which can cause potentially serious complications including shortness of breath and pulmonary hypertension.[12]

SS can cause significant physical symptoms and disability as described above, however SS can also cause other reductions in quality of life. A 2007 qualitative study found that symptoms such as pain and fatigue had a major influence on daily activities and quality of life. All of the study participants reported significant disruption to their social life and wellbeing because of emotional distress, depression, low self-esteem, concerns with physical appearance and uncertainty about the future.[13]

## CLINICAL NEED and BURDEN OF DISEASE

An estimated two and a half million people worldwide and around 12,000 in the UK are diagnosed with scleroderma.[14]

Diffuse cutaneous SS (dcSS) is rare condition with an estimated prevalence of 1 per 25,000. Women are more likely than men to develop dcSS with a female/male gender ratio of approximately 4 to1.[15]

Prognosis of dcSS can range from severe symptoms to the risk of life threatening complications.[15] 10-year survival rate for dcSS is estimated at 60-80%.[15] Improvements in 5-year survival of dcSS have been observed, with an increase from 69% in 1990-1993 to 84% in 2000-2003.[16]

Severe life threatening complications can occur in dcSS, including renal involvement (occurring in 2% dcSS cases), pulmonary fibrosis (seen in 60% dcSS cases) and pulmonary hypertension (occurring in 10-15% dcSS cases).[15]

# PATIENT PATHWAY

## RELEVANT GUIDANCE

### NICE GUIDANCE

No relevant guidance identified.

### NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a
- NHS England. Clinical Commissioning Policy: Sildenafil and Bosentan for the Treatment of Digital Ulceration in Systemic Sclerosis. NHS England: A13/P/b. July 2015.

### OTHER GUIDANCE

NICE Evidence Summary. *ES7: Skin involvement in systemic sclerosis: rituximab*. March 2017.[17]

British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR). *BSR and BHPR guideline for the treatment of systemic sclerosis*. October 2016.[18]

European League Against Rheumatism (EULAR). *Update of EULAR recommendations for the treatment of systemic sclerosis*. October 2016.[19]

NICE Evidence Summary. *ESUOM32: Scleroderma: oral mycophenolate*. July 2014.[20]

## CURRENT TREATMENT OPTIONS

There is no cure for SS and the aim of treatment is to relieve symptoms, prevent disease progression and treat complications. Therefore, treatments will vary depending on what is being experienced by the patient. An overview of the treatment options for the main symptoms, prevention of disease progression and complications of SS are as follows:[21, 22]

*Treating symptoms*

- Treatment for Raynaud's phenomenon: drugs to widen the blood vessels (e.g. nifedipine) and therefore improve circulation can be given (often several at a time). In severe cases (with ulcers which will not heal) iloprost may be given.
- Treatment for heartburn/swallowing difficulties: Antacids or proton pump inhibitors (PPIs) may be prescribed for long term treatment (months/years).
- Treatment for gastrointestinal symptoms: symptoms such as diarrhoea and anal incontinence may need follow up with a gastroenterologist.
- Treatment for inflamed joints: painkillers and NSAIDs may be prescribed at the lowest effective dose for the shortest period of time.[21, 22]

*Preventing disease progression*

Medications to supress the immune system may be used to lower the immune response in SS. These can include steroid tablets which are usually given in the early stages of the disease or later in the

disease to treat inflammation in the muscles or lungs. Immunosuppressant drugs (e.g. methotrexate, cyclophosphamide, azathioprine and mycophenolate) may be given in more severe cases of SS, especially in cases where there is extensive skin or lung disease.[21, 22]

*Treating complications*

- Skin complications: dressings and antibiotics may be used for kin ulcers and surgery may be needed for tight skin, nodules or ulcers.
- Lung and heart complications: lung inflammation may be treated with steroid tablets of disease modifying anti-rheumatic drugs (DMARDs). Pulmonary hypertension can be treated with several drugs (e.g. Bosentan, abrisentan, sildenafil or iloprost) which can improve symptoms.
- Treatment for hypertension and kidney complications: ACE inhibitors to control blood pressure.
- Thyroid complications: Thyroid hormone replacement tablets may be given to those with underactive thyroid.
- Impotence: sildenafil and tadalafil may be prescribed for erectile problems.
- Infections: as SS may cause susceptibility to infections so antibiotics are needed promptly for any infections.[21, 22]

Lifestyle changes can also help to minimise disability in SS and are recommended. These can include:

- Regular physiotherapy and stretching exercises to keep muscles supple, keep joints mobile and loosen tight skin.
- Occupational therapy to advise on aids (e.g. splints to support the joints) and help with daily living tasks.
- Wearing thick gloves or socks to keep hands/feet warm in those with Raynaud's phenomenon.
- Healthy eating, regular exercise and smoking cessation (for those who smoke) to control blood pressure and improve circulation.
- Patient information and support groups to provide understanding of the disease and how to effectively manage the condition.[22, 12]

## EFFICACY and SAFETY

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| **Trial** | RESOLVE-1, NCT03398837; lenabasum vs placebo, phase III |
| **Sponsor** | Corbus Pharmaceuticals Inc. |
| **Status** | ongoing - recruiting |
| **Source of Information** | trial registry[2] |
| **Location** | USA |
| **Design** | Randomised, double blind, placebo-controlled |
| **Participants** | n= 354 (planned); aged 18 years and older; diffuse cutaneous systemic sclerosis; disease duration less than 6 years (from first non-Raynaud symptom); no new/increased dose immunosuppressive medication within 8 weeks prior to screening |
| **Schedule** | Participants are randomised to one of three treatment arms: |

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| | 1. Lenabasum 5mg twice daily<br>2. Lenabasum 20mg twice daily<br>3. Placebo capsule twice daily |
| **Follow-up** | Follow-up for up to 1 year |
| **Primary Outcomes** | Efficacy of lenabaum compared to placebo for change from baseline in Rodnan skin score (RSS) (baseline to up to 1 year) – RSS evaluates a subject's skin thickness on a 4 point scale for 17 surface anatomic areas (0 = normal skin; 1 = mild thickness; 2 = moderate thickness; 3 = severe thickness with inability to pinch skin into fold). The individual values of the 17 surface areas are summed to define the total skin score with a maximum score of 51. |
| **Secondary Outcomes** | Efficacy of lenabasum compared to placebo for change from baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI) (baseline up to 1 year) - includes 8 sections: dressing, arising, eating, walking, hygiene, reach, grip, and activities. There are 2 or 3 questions for each section. Scoring within each section is from 0 (without any difficulty) to 3 (unable to do). The individual scores of the eight sections are summed and divided by 8. The result is the disability index or functional disability index. A higher score indicates more functional disability.<br><br>Efficacy of lenabasum compared to placebo for the American College of Rheumatology Combined Response Index in diffuse cutaneous Systemic Sclerosis score (baseline to up to 1 year) - The ARC CRISS exponential algorithm determines the predicted probability of improvement from baseline, incorporating change in RSS, FVC % predicted, physician and patient global assessments, and HAQ-DI. The outcome is a continuous variable between 0.0 and 1.0 (0 - 100%). A higher score indicates greater improvement.<br><br>Efficacy of lenabasum compared to placebo for change from baseline in forced vital capacity (baseline to up to 1 year). |
| **Key Results** | - |
| **Adverse effects (AEs)** | - |
| **Expected reporting date** | Estimated primary completion date: March 2020<br>Estimated completion date: March 2020 |

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| **Trial** | NCT02465437; lenabasum vs placebo; phase II |
| **Sponsor** | Corbus Pharmaceuticals Inc. |
| **Status** | published in abstract |
| **Source of Information** | abstract[23], press release[24], presentation[25], trial registry[26] |
| **Location** | USA |
| **Design** | Randomised, double blind, placebo-controlled |
| **Participants** | n=42; aged 18-70 years; diffuse cutaneous systemic sclerosis; disease duration less than 3 years from the first non-Raynaud's phenomenon or between 3 and 6 years from the first non-Raynaud's phenomenon and high sensitivity C-reactive protein > 3 mg/L, high sensitivity interleukin-6 > 5 pg/mL, or increase in RSS ≥ 5 points over the last 6 months with total RSS ≥ 12; stable treatment for SSc for at least 28 days before Visit 1 |

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| **Schedule** | There are 2 parts to this study, Part A (a randomised placebo controlled trial) and Part B (open label extension).<br>During Part A, participants are randomised to one of four treatment arms:<br>1. Lenabasum 5mg in the morning followed by 20 mg in the evening on days 1-28 then lenabasum 20mg twice per day on days 29-84.<br>2. Lenabasum 20mg in the morning followed by 20mg in the evening on days 1-28 then lenabasum 20mg twice per day on days 29-84.<br>3. Lenabasum 20mg twice per day on days 1-84.<br>4. Placebo twice per day on days 1-84.<br>During Part B, participants who have completed Part A without permanent discontinuation of the drug and pass repeat safety screening (screening period up to 28 days) are eligible for enrolment. 20mg of lenabasum was given twice per day for days 1-364. |
| **Follow-up** | Part A: active treatment for 84 days followed by 28 day follow up period<br>Part B: active treatment for 364 days followed by 28 day follow up period |
| **Primary Outcomes** | Number of participants with treatment-emergent adverse events from baseline at day 113 (Part A – 84 day treatment and 28 day follow up)<br><br>Change in Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) from baseline to day 85 (Part A – 84 day treatment) (CRISS responders and its domains of modified Rodnan skin score, forced vital capacity percent predicted, Physician Global Assessment, Patient Global Assessment, and Health Assessment Questionnaire Disability-Index)<br><br>Number of participants with treatment-emergent adverse events from baseline to day 394 (Part B – 365 treatment days and 28 day follow up)<br><br>Change in CRISS from baseline to day 394 (Part B – 365 treatment days and 28 day follow up) |
| **Secondary Outcomes** | Change in patient reported outcomes from baseline to day 85 (84 day treatment period). Outcomes include: National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS)-29 Short Form, the PROMIS-29 Short Form single item pain numerical rating score, the 5-D Itch Score, and a Systemic Sclerosis Skin Questionnaire.<br><br>Change in lenabasum plasma concentrations from baseline to day 85 (84 day treatment period)<br><br>Change in metabolipidomic profile from baseline to day 85 (84 day treatment period)<br><br>Change in blood biomarkers of disease activity, inflammation and fibrosis from baseline to day 84 (84 day treatment period)<br><br>Change in skin biomarkers of inflammation and fibrosis from baseline to day 85 (84 day treatment period) |
| **Key Results** | Corbus Pharma reported that the difference between the lenabasum (n=26) and placebo (n=15) in CRISS score over the trial period was significant (p=0.044). Median CRISS Score (25$^{th}$ percentile, 75$^{th}$ percentile) was 33% (0.8%, 82.1%) in |

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| | the lenabasum group at week 16 compared to 0% (0.1%, 16%) in the placebo group at week 16.[24]<br>36/38 (95%) participants from Part A were recruited into Part B (open label extension - OLE) of the study. The median duration of OLE was 194 days. After 10 weeks of lenabasum treatment in the OLE, mean RSS declined by -3.2 (±3.9) compared to baseline (p=0.0001).[23] |
| **Adverse effects (AEs)** | No serious, severe or unexpected adverse events were related to lenabasum occurred during Part A of the study. 1/27 (3.7%) participants taking lenabasum developed an AE and withdrew from the study due to moderate dizziness.[24]<br>Treatment emergent AEs (TEAEs) occurred in n=13 (48%) in the lenabasum group compared to n=6 (40%) in the placebo group between week 1-4. TEAEs occurred in n=12 (44%) in the lenabasum group compared to n=6 (40%) in the placebo group during week 5 -12. The most common AEs recorded during Part A of the study were dizziness (22% lenabasum participant's vs 13% placebo participants) and fatigue (19% lenabasum participant's vs 7% placebo participants).[25]<br>In Part B (OLE study, n=36), most AEs were mild (55/88, 62%) or moderate (30/88, 34%) in severity and classed as unrelated to lenabasum (75/88, 85%). The most common AEs (occurring in >10% participants) were mild fatigue (n=5, 14%) and mild/moderate upper respiratory tract infection (n=4, 11%). Dizziness occurred in n=2 participants (6%). One participant developed renal crisis 7 days after starting 60mg/day prednisone prescribed by a non-study doctor resulting in two severe and 1 life threatening/serious AE.[23] |
| **Expected reporting date** | - |

## ESTIMATED COST and IMPACT

### COST

The cost of lenabasum is not yet known.

### IMPACT – SPECULATIVE

### IMPACT ON PATIENTS AND CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☐ Other

☐ No impact identified

### IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☒ Decreased use of existing services

☐ Re-organisation of existing services

☐ Need for new services

☐ Other

☐ None identified

## IMPACT ON COSTS and OTHER RESOURCE USE

☐ Increased drug treatment costs

☐ Reduced drug treatment costs

☐ Other increase in costs

☒ Other reduction in costs: *potentially reduced symptoms and disease progression leading to reduced need for other treatments*

☐ Other

☐ None identified

## OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

## REFERENCES


[1] Corbus Pharmaceuticals. *Lenabasum*. Available from: https://www.corbuspharma.com/pipeline/lenabasum [Accessed 27 February 2018]

[2] ClinicalTrials.gov. *Trial to Evaluate Efficacy and Safety of Lenabasum in Diffuse Cutaneous Systemic Sclerosis (RESOLVE-1).* Available from: https://clinicaltrials.gov/ct2/show/NCT03398837 [Accessed 27 February 2018]. Last Updated 22 February 2018

[3] ClinicalTrials.gov. *Safety, Tolerability, Pharmacokinetics, and Efficacy of JBT-101 in Cystic Fibrosis*. Available from: https://clinicaltrials.gov/ct2/show/NCT02465450 [Accessed 27 February 2018]. Last Updated 9 February 2018

[4] ClinicalTrial.gov. Safety, Tolerability, and Efficacy of JBT-101 in Subjects With Dermatomyositis. Available from: https://clinicaltrials.gov/ct2/show/NCT02466243 [Accessed 27 February 2018]. Last Updated 11 September 2017

[5] ClinicalTrials.gov. *JBT-101 in Systemic Lupus Erythematosus (SLE)*. Available from: https://clinicaltrials.gov/ct2/show/NCT03093402 [Accessed 27 February 2018]. Last Updated 27 December 2017

[6] Global Data. *Opportunity Analyzer: Systemic Sclerosis (Scleroderma) – Opportunity Analysis and Forecast to 2024.* December 2015. Available from: https://pharma.globaldata.com/Reportsview.aspx?DocID=47457 [Accessed 6 March 2018] Login Required

[7] European Medicines Agency. *EU/3/16/1808*. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2017/07/human_orphan_001992.jsp&mid=WC0b01ac058001d12b [Accessed 27 February 2018]

[8] Corbus Pharmaceuticals. *Corbus Pharmaceuticals Announces FDA Orphan Drug Designation for Resunab(TM) for the Treatment of Systemic Sclerosis (Scleroderma)*. Available from: https://www.corbuspharma.com/news/press-releases/detail/184/corbus-pharmaceuticals-announces-fda-orphan-drug [Accessed 27 February 2018]

[9] Corbus Pharmaceuticals. *Corbus Pharmaceuticals' Investigational Drug Resunab(TM) Granted Fast Track Status by the U.S. FDA for the Treatment of Systemic Sclerosis*. Available from: https://ir.corbuspharma.com/press-releases/detail/191/corbus-pharmaceuticals-investigational-drug-resunabtm [Accessed 27 February 2018]

[10] Arthritis Research UK. *What is systemic sclerosis (scleroderma)?* Available from: https://www.arthritisresearchuk.org/arthritis-information/conditions/systemic-sclerosis/what-is-scleroderma.aspx [Accessed 27 February 2018]

[11] I Badea, M Taylor, A Rosenberg, M Foldvari; Pathogenesis and therapeutic approaches for improved topical treatment in localized scleroderma and systemic sclerosis. *Rheumatology*. Volume 48, Issue 3, 1 March 2009, Pages 213–221, https://doi.org/10.1093/rheumatology/ken405

[12] NHS Choices. *Scleroderma.* Available from: https://www.nhs.uk/conditions/scleroderma/#types-of-scleroderma-and-typical-symptoms [Accessed 6 March 2018]

[13] ME Suarez-Almazor, MA Kallen, AK Roundtree, M Mayes. Disease and symptom burden in systemic sclerosis: a patient perspective. *J Rheumatol*. 2007 Aug;34(8):1718-26. Epub 2007 Jul 1.

[14] Scleroderma & Raynaud's UK. *What is Scleroderma?* Available from: https://www.sruk.co.uk/scleroderma/what-scleroderma/ [Accessed 6 March 2018]

[15] Orphanet. *Diffuse cutaneous systemic sclerosis.* Available from: http://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=18905&Disease_Disease_Search_diseaseGroup=systemic-sclerosis&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group of diseases=Diffuse-cutaneous-systemic-sclerosis&title=Diffuse-cutaneous-systemic-sclerosis&search=Disease_Search_Simple [Accessed 6 March 2018]

[16] SI Nihtyanova, EC Tang, JG Coghlan, AU Wells, CM Black, CP Denton. Improved survival in systemic sclerosis is associated with better ascertainment of internal organ disease: a retrospective cohort study. *QJM*. 2010 Feb;103(2):109-15. doi: 10.1093/qjmed/hcp174.

[17] NICE Evidence Summary. *ES7 Skin involvement in systemic sclerosis: rituximab.* March 2017. Available from: https://www.nice.org.uk/advice/es7/chapter/Key-points [Accessed 27 February 2018]

[18] CP. Denton, M Hughes, N Gak, J Vila, M H. Buch, K Chakravarty, *et al*. BSR and BHPR guideline for the treatment of systemic sclerosis, *Rheumatology*, Volume 55, Issue 10, 1 October 2016, Pages 1906–1910. https://doi.org/10.1093/rheumatology/kew224

[19] O Kowal-Bielecka, J Fransen, J Avouac, M Becker, A Kulak, Y Allanore, *et al.* Update of EULAR recommendations for the treatment of systemic sclerosis. *Ann Rheum Dis.* Volume 76, Issue 8, August 2017, Pages 1327-1339. doi:10.1136/annrheumdis-2016-209909

[20] NICE Evidence Summary. *ESUOM32 Scleroderma: oral mycophenolate.* July 2014. Available from: https://www.nice.org.uk/advice/esuom32/chapter/Key-points-from-the-evidence [Accessed 27 February 2018]

[21] Arthritis Research UK. *Systemic Sclerosis (scleroderma): What treatments are there?* Available from: https://www.arthritisresearchuk.org/arthritis-information/conditions/systemic-sclerosis/treatments.aspx [Accessed 6 March 2018]

[22] Scleroderma & Raynaud's UK. *Systemic Sclerosis – Treatments*. Available from: https://www.sruk.co.uk/scleroderma/scleroderma-treatments/systemic-sclerosis-treatments/ [Accessed 6 March 2018]

[23] American College of Rheumatology (ACR/ARHP) Annual Meeting, November 3 - 8 in San Diego, California. Abstract Number: 725. *Safety and Efficacy of Anabasum (JBT-101) in Diffuse Cutaneous Systemic Sclerosis (dcSSc) Subjects Treated in an Open-Label Extension of Trial JBT101-SSc-001*. Available from: http://acrabstracts.org/abstract/safety-and-efficacy-of-anabasum-jbt-101-in-diffuse-cutaneous-systemic-sclerosis-dcssc-subjects-treated-in-an-open-label-extension-of-trial-jbt101-ssc-001/ [Accessed 6 March 2018]

[24] Corbus Pharmaceuticals. *Corbus Pharmaceuticals Reports Positive Topline Results Showing Clear Signal of Clinical Benefit with Resunab (JBT-101) in Phase 2 Study in Systemic Sclerosis.* 14 November 2016. Available from: https://www.corbuspharma.com/news/press-releases/detail/221/corbus-pharmaceuticals-reports-positive-topline-results [Accessed 27 February 2018]

[25] R Spiera *et al*. A Phase 2 Study of the Safety and Efficacy of Anabasum (JBT-101) in Systemic Sclerosis. Presented at the 13th Annual European Congress of Rheumatology - European League Against Rheumatism (EULAR), June 14 - 17, 2017, Madrid, Spain. Available from: http://c.eqcdn.com/corbuspharma/db/184/2050/pdf/EULAR_Presentation_6.15.17_w.pdf [Accessed 27 February 2018]

[26] ClinicalTrials.gov. *Safety, Tolerability, Efficacy, and Pharmacokinetics of JBT-101 in Systemic Sclerosis*. Available from: https://www.clinicaltrials.gov/ct2/show/NCT02465437 [Accessed 27 February 2018]. Last Updated 23 October 2017