AI generated - may have errors

Strategic context:

Standardized Medical Name: Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)

Target Patient Profile:

- **Temporality:** Prevalent
- **Disease Stage/State:** Active SSc-ILD. This encompasses the broad spectrum of the disease, including patients initiating therapy, those stable on current standard of care (e.g., mycophenolate mofetil, nintedanib, tocilizumab), and those exhibiting evidence of disease progression despite treatment (Progressive Pulmonary Fibrosis phenotype).

Strategic Rationale: Pharmaceutical Relevance (2025-2026):

Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD) remains the primary driver of mortality in patients with Systemic Sclerosis. While the current standard of care—immunosuppression combined with targeted therapies (Nintedanib and Tocilizumab)—slows the rate of lung function decline, these treatments do not halt or reverse fibrosis. A substantial unmet need persists for therapies with superior efficacy, particularly for the significant subset of patients who continue to progress despite available treatments.

The 2025-2026 pharmaceutical agenda is intensely focused on introducing next-generation therapies and novel mechanisms of action. The strategic focus is bifurcated between aggressively targeting the progressive fibrotic phenotype (PPF) and modulating the underlying immune dysregulation driving the disease.

Key evidence demonstrating high strategic relevance and developments shaping the 2025-2026 landscape include:

- **Imminent Launch Targeting Progressive Pulmonary Fibrosis (PPF):** The most significant development for this horizon is Boehringer Ingelheim's **Nerandomilast (BI 1015550)**, a preferential PDE4B inhibitor. The Phase III FIBRONEER-ILD trial, evaluating Nerandomilast in patients with PPF (including progressive SSc-ILD), met its primary endpoint. Following the presentation of full data in Q2 2025, regulatory filings are underway. The anticipated market entry of Nerandomilast in late 2025/2026 will likely reshape the treatment paradigm for patients progressing on current therapies.
- **Late-Stage B-Cell Modulation:** Recognizing the autoimmune drivers of SSc, targeted immunomodulation remains critical. GSK is advancing **Belimumab** (anti-BAFF/BLyS inhibitor) in a dedicated Phase III program for SSc-ILD (NCT05878717). This represents a major late-stage investment, with the trial actively ongoing throughout 2025-2026 and data anticipated shortly thereafter.

- **Novel Inflammation Resolution Pathways:** The industry is exploring first-in-class mechanisms aimed at resolving inflammation without broad immunosuppression. aTyr Pharma's **Efzofitimod**, a neuropilin-2 (NRP2) modulator, is in the Phase II EFZO-CONNECT study. Following positive interim data in June 2025, primary lung function endpoint data is expected in late 2025 or 2026.
- **Platform Trial Innovation:** The CONQUEST platform trial (NCT06195072) is actively investigating agents such as Amlitelimab (anti-OX40L) and Nerandomilast specifically in SSc-ILD during 2025-2026, highlighting the industry's commitment to efficient evaluation of novel mechanisms in this population.

Intended Clinical Application Research Utility:

Epidemiological research on a prevalent SSc-ILD cohort is essential to support the market access, strategic positioning, and comparative effectiveness analysis of late-stage and newly launched assets (e.g., Nerandomilast, Belimumab, Efzofitimod). Key research utilities include characterizing contemporary real-world treatment patterns (including utilization and sequencing of nintedanib, tocilizumab, and background immunosuppressants), defining the residual unmet need by quantifying the rate of FVC decline in patients receiving current standard of care, and accurately identifying the proportion of SSc-ILD patients who meet the criteria for Progressive Pulmonary Fibrosis (PPF) to define the addressable market for emerging PPF-targeted therapies.

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Clinical Description: Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD) – Incident

Synonyms: Scleroderma Lung Disease; SSc-ILD; New-onset ILD secondary to Systemic Sclerosis.

1. Clinical Case Definition

This phenotype specifically captures the *initial onset* or *first clinical recognition* (incidence) of Interstitial Lung Disease in a patient with either established or concurrently diagnosed Systemic Sclerosis (SSc). SSc-ILD is a manifestation of SSc, an autoimmune connective tissue disease, characterized by inflammation and progressive fibrosis of the pulmonary parenchyma (the interstitium).

The diagnosis requires confirmation of both components:

- **Systemic Sclerosis** is diagnosed based on established clinical features (e.g., skin thickening/sclerodactyly, Raynaud's phenomenon) and supportive autoantibodies (e.g., anti-Scl-70/topoisomerase I, anti-centromere, or anti-RNA polymerase III).
- **Incident Interstitial Lung Disease** is identified by new evidence of pulmonary involvement. This is typically established using High-Resolution Computed Tomography (HRCT) of the chest, demonstrating findings such as ground-glass opacities, reticulation, traction bronchiectasis, or honeycombing, often in patterns consistent with Non-Specific Interstitial Pneumonia (NSIP) or Usual Interstitial Pneumonia (UIP). Pulmonary Function Tests (PFTs) support the diagnosis by revealing a restrictive ventilatory defect (reduced Forced Vital Capacity (FVC)) and/or impaired gas exchange (reduced Diffusion Capacity for Carbon Monoxide (DLCO)).

2. Phenotype Scope & Granularity

- **Temporal Context:** Incident. Intended to identify the new onset or first clinical recognition of ILD in the context of SSc.
- **Severity:** Broad spectrum. Inclusive of all severities present at the time of initial diagnosis, ranging from subclinical radiographic findings to symptomatic and physiologically significant disease.
- **Acuity / Chronicity:** Represents the onset of a chronic pulmonary manifestation (ILD) within the context of an underlying chronic systemic disease (SSc).
- **Etiology:** Autoimmune; specifically secondary to Systemic Sclerosis.
- **Population Context:** Primarily the adult population.

3. Related Conditions & Scope Boundaries

This phenotype specifically requires the identification of new-onset ILD secondary to Systemic Sclerosis.

- **Prevalent SSc-ILD / Prior History of SSc-ILD:** Patients with a pre-existing diagnosis of SSc-ILD before the observation period are not within the scope of this *incident* phenotype.
- **Idiopathic Pulmonary Fibrosis (IPF):** IPF is a distinct form of ILD occurring without an associated systemic autoimmune disease and is not within the scope of this phenotype.
- **Other Connective Tissue Disease-associated ILD (CTD-ILD):** ILD associated with other systemic diseases (e.g., Rheumatoid Arthritis, Myositis, Sjögren's Syndrome) are distinct etiologies and are not within the scope of this SSc-specific phenotype.
- **Exposure-related or Drug-induced ILD:** ILD caused primarily by environmental exposures (e.g., hypersensitivity pneumonitis) or medications are etiologically distinct and not within the scope of SSc-ILD.
- **Systemic Sclerosis without ILD:** Patients with SSc who have not yet developed interstitial lung involvement are not the target population for this phenotype definition.
- **Other Pulmonary Manifestations of SSc:** While SSc can cause Pulmonary Arterial Hypertension (PAH) or aspiration pneumonia, these are distinct pathophysiological processes (vasculopathy or aspiration vs. parenchymal fibrosis) and are not sufficient alone to meet this phenotype definition.

4. Key Complications & Common Comorbidities

These conditions frequently co-occur with SSc-ILD or are complications of SSc, but they are distinct clinical entities from the interstitial lung pathology itself.

- **Pulmonary Hypertension (PH) / Pulmonary Arterial Hypertension (PAH):** A frequent and significant vascular complication/comorbidity.
- **Gastroesophageal Reflux Disease (GERD) and Esophageal Dysmotility:** Highly prevalent in SSc and may exacerbate lung injury via aspiration.
- **Raynaud’s Phenomenon and Digital Ulcers:** Common vascular manifestations of the underlying SSc.
- **Scleroderma Renal Crisis:** A specific renal complication of SSc.
- **Cardiac Involvement:** Including myocarditis, pericardial effusion, or heart failure.

5. Intended Data Sources

This clinical description is intended for building concept sets against real-world administrative claims, electronic health record (EHR) databases, and patient registries. The target data should be standardized to the OMOP Common Data Model. Examples of licensable data sources where this concept set would be applied include:

- **Optum®** (Clinformatics® Data Mart, SES, Pan-Therapeutic)
- **Merative™** (MarketScan® Commercial Claims and Encounters)
- **Veradigm** (Health Verity, Practice Fusion EHR)
- **IQVIA** (AmbEMR, PharMetrics Plus)
- **HealthVerity**