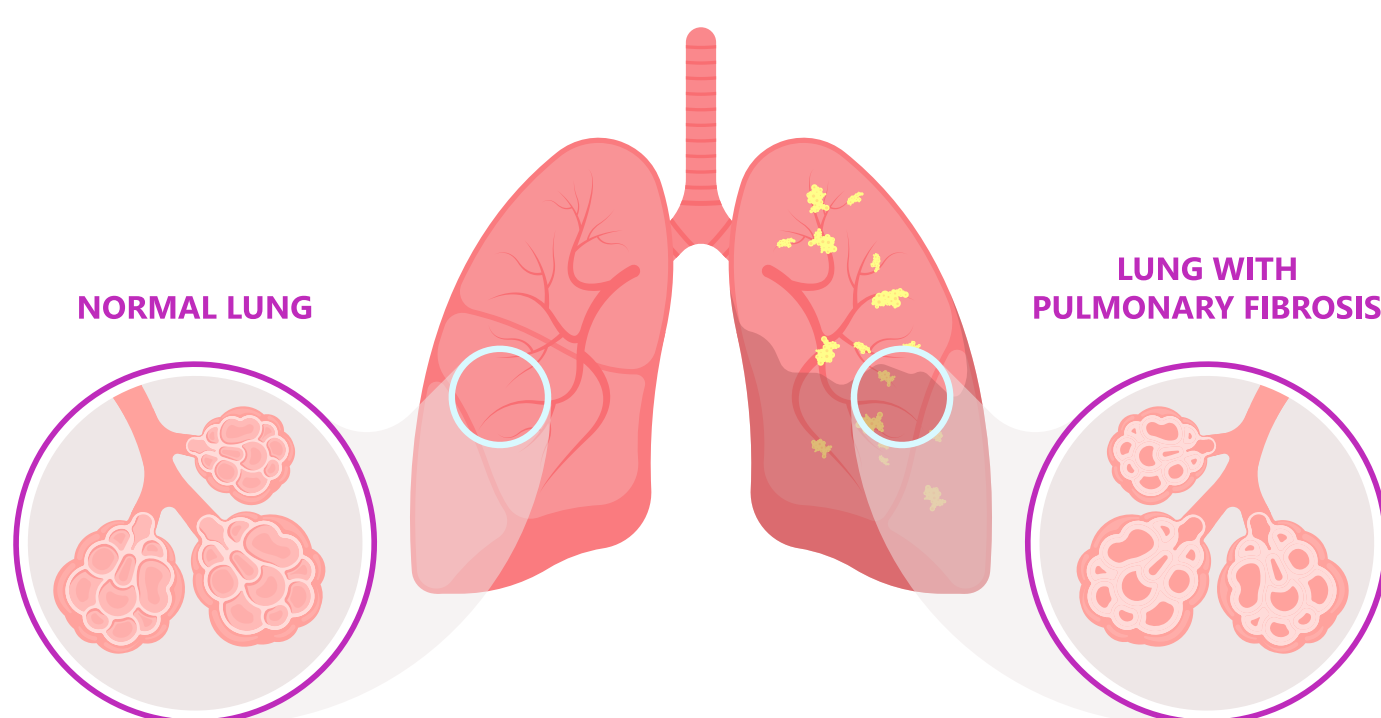


Lysophosphatidic acid receptor 1 (LPA₁) in pulmonary fibrosis

While currently approved therapies can slow the decline in lung function caused by pulmonary fibrosis (PF), unmet needs remain. Fueled by our passion to help more patients, we are driven to tailor treatments to individual needs and help relieve the burdens of immune-mediated diseases such as pulmonary fibrosis.

Understanding pulmonary fibrosis

Pulmonary fibrosis (fibrosis occurring in the lungs) is a chronic, life-threatening interstitial lung disease (ILD) that is associated with worsening respiratory symptoms and reduced quality of life.^{1,2}



Fibrosis is defined by the overgrowth, hardening and/or scarring of various tissues.¹ It can occur in virtually any organ and results from inflammation that may be caused by a number of factors.^{1,3}

Pulmonary fibrosis occurs when lung tissue becomes damaged and scarred, reducing the lungs' ability to expand, collapse and, ultimately, function effectively.⁴⁻⁶ The disease can lead to respiratory failure and death.^{1,2}

Understanding PF subtypes: PPF and IPF

Progressive pulmonary fibrosis (PPF) is the preferred term to describe patients that have ILD with a progressive fibrotic phenotype.⁷



Idiopathic pulmonary fibrosis (IPF) is the **most common type of progressive fibrosing ILD**.¹ As an idiopathic disease, there is no identifiable cause.



Many people living with PPF and IPF are **physically impaired**, experience a **progressive decline in lung function**, have difficulty performing simple daily activities due to **breathlessness** and require **continuous supplemental oxygen** to ease the burden of normal breathing.

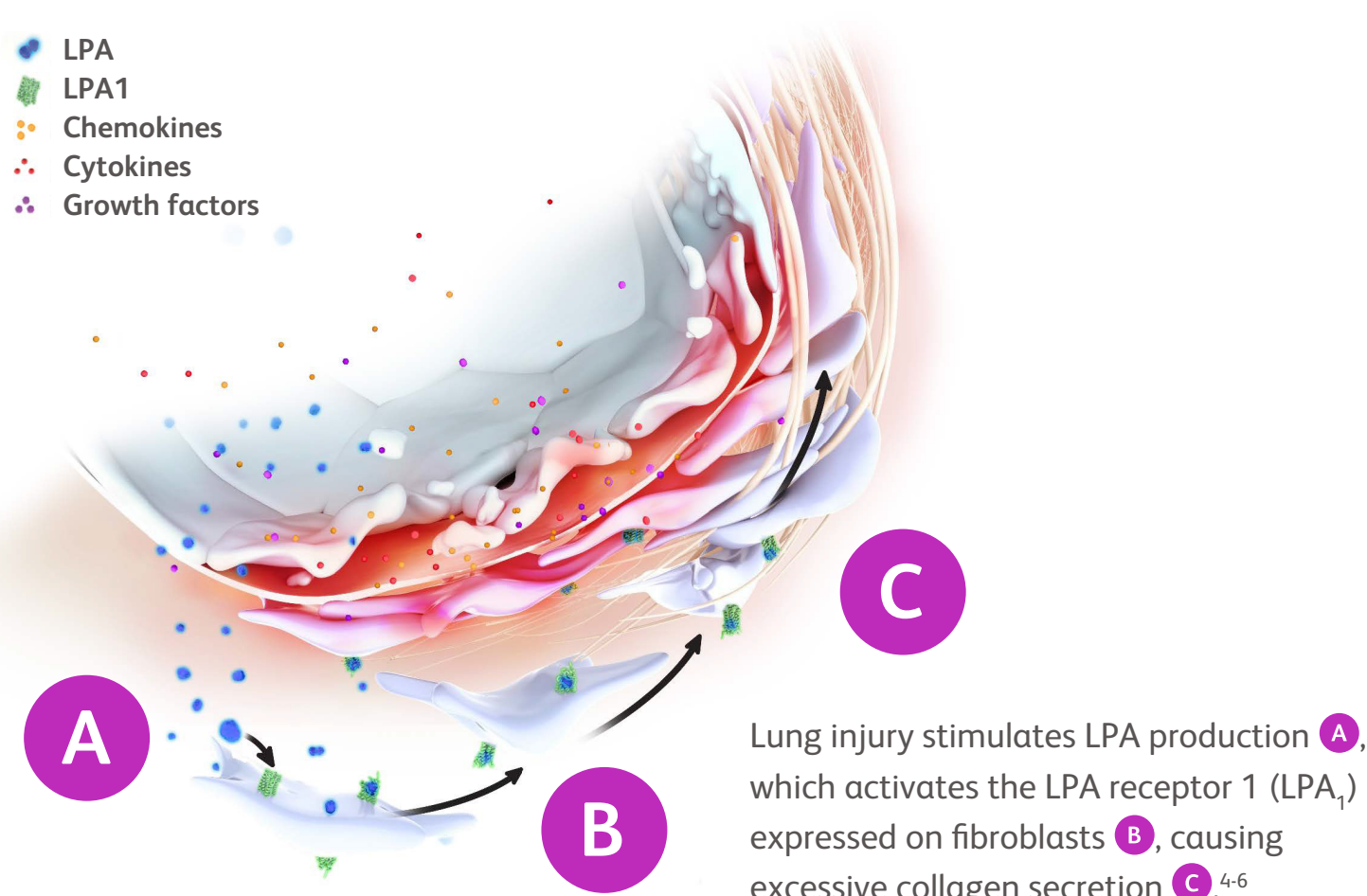


IPF is a fatal disease with a **median survival time of 3 to 5 years** following diagnosis and a **5-year survival rate of approximately 45%**. Innovation in treatment has been limited with few new therapies approved in **nearly 10 years**.

As a result, a significant need exists for new therapies.⁸

LPA in pulmonary fibrosis

Lysophosphatidic acid (LPA) promotes wound healing and collagen deposition.



Increased LPA levels and activation of LPA₁ have been implicated in the pathogenesis of pulmonary fibrosis.⁹

A preclinical *in vitro* and *in vivo* study found that antagonizing—or blocking—LPA₁ receptors may have an impact in treating lung injury and fibrosis.⁵

At Bristol Myers Squibb, we pursue **strategic research approaches to address unmet needs for patients**. We understand how fibrosis plays a role in the development of several immune-mediated diseases and are applying this knowledge to develop new treatments that we hope may **address the underlying causes of disease**.

1. Wynn TA. Cellular and molecular mechanisms of fibrosis. *J Pathol*. 2008;214(2):199-210. doi:10.1002/path.2277
2. Selman M, Pardo A. From pulmonary fibrosis to progressive pulmonary fibrosis: A lethal pathobiological jump. *Am J Physiol Lung Cell Mol Physiol*. 2021;321(3):L600-L607. doi:10.1152/ajplung.00310.2021
3. Rockey DC, Bell PD, Hill JA. Fibrosis—a common pathway to organ injury and failure. *N Engl J Med*. 2015;372(12):1138-1149. doi:10.1056/NEJMr1300575
4. Ahluwalia N, Shea BS, Tager AM. New therapeutic targets in idiopathic pulmonary fibrosis. Aiming to rein in runaway wound-healing responses. *Am J Respir Crit Care Med*. 2014;190(8):867-878. doi:10.1164/rccm.201403-0509PP
5. Swaney JS, Chapman C, Correa LD, et al. A novel, orally active LPA(1) receptor antagonist inhibits lung fibrosis in the mouse bleomycin model. *Br J Pharmacol*. 2010;160(7):1699-1713. doi:10.1111/j.1476-5381.2010.00828.x
6. Ito JT, Lourenço JD, Righetti RF, Tibério I, Prado CM, Lopes F. Extracellular matrix component remodeling in respiratory diseases: What has been found in clinical and experimental studies? *Cells*. 2019;8(4).
7. Raghu G, Remy-Jardin M, Richeldi L, et al. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults: An official ATS/ERS/JRS/Alat clinical practice guideline. *Am J Respir Crit Care Med*. 2022;205(9). doi:10.1164/rccm.202202-0399st
8. Maher TM, Strek ME. Antifibrotic therapy for idiopathic pulmonary fibrosis: time to treat. *Respir Res*. 2019;20(1):205. doi:10.1186/s12931-019-1161-4
9. Smith RA, Kim J, Donnelly DJ, et al. BMS-986327 as a novel PET imaging agent for assessment of LPA1 receptors in IPF. Poster presented at: European Respiratory Society (ERS) International Congress; September 28-October 2, 2019; Madrid, Spain.