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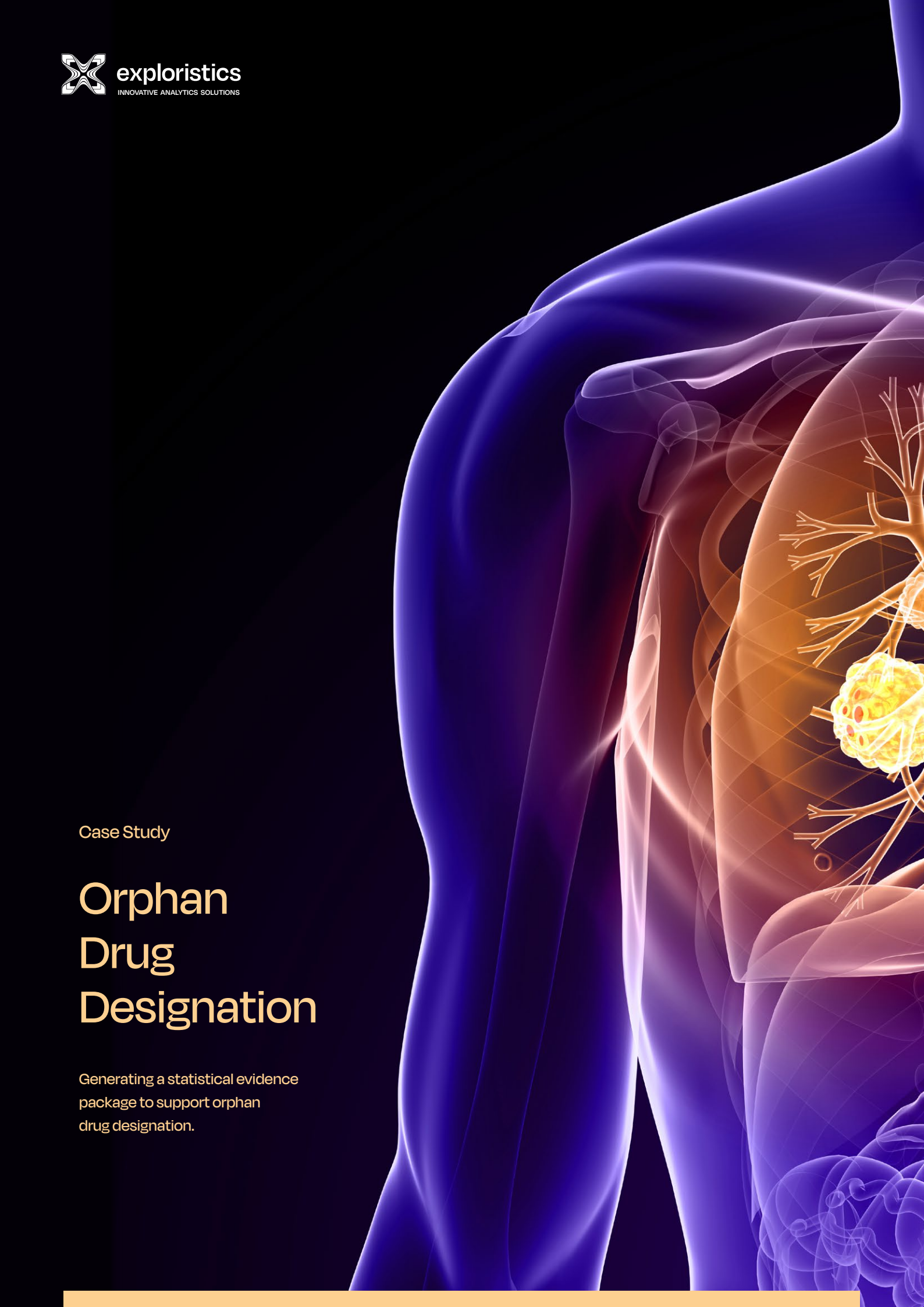
INNOVATIVE ANALYTICS SOLUTIONS



Case Study

# Orphan Drug Designation

Generating a statistical evidence package to support orphan drug designation.

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## The Challenge

Idiopathic Pulmonary Fibrosis (IPF) is a debilitating condition in which breathing becomes increasingly difficult due to chronic lung scarring (**Figure 1**). A privately held biotechnology company focused on the development of novel treatments for fibrosis and cancer sought orphan drug designation from both the EMA (European Medicines Agency) and FDA (U.S. Food and Drug Administration) for a new investigative agent as a candidate IPF treatment.

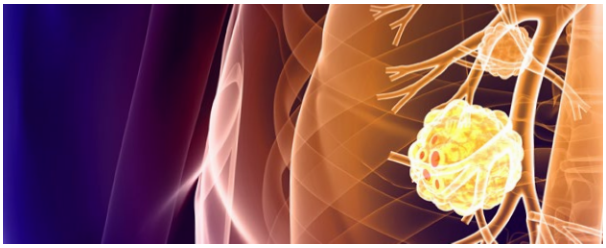

**Figure 1.** Scarring of lung alveoli obstructs breathing in IPF.

The investigative agent had shown a significant reduction in chitinase-like protein YKL-40, a serum biomarker in diseases with fibrosis, inflammation and tissue remodeling, as well as other biomarkers relevant to IPF in its first-in-human clinical study in IPF patients after 14 days of treatment. No changes in YKL-40 were reported in a study of patients being treated with the current approved treatments pirfenidone and nintedanib, alone or in combination.

To qualify for orphan drug designation both the investigative agent and clinical condition needed to meet criteria specified by each regulatory agency. In the EU, a rare or orphan disease must have a prevalence of no more than 50 per 100,000 person-years, while in the US it must affect fewer than 200,000 people in the total population.

## The Approach

To show that IPF met both the EMA and FDA definitions of an orphan disease and that therefore the investigative agent was a candidate orphan drug, an extensive systematic literature review was carried out to identify publications containing IPF prevalence data which were used to create separate US and EU datasets. For each regulatory jurisdiction, a dataset was generated containing the prevalence rate, number of IPF cases, total population-years, and subgroup details (age category, gender, calendar year) per publication. These datasets were then used to examine the:

- time periods over which the publications collected data
- overall prevalence rate in each age category by gender
- overall prevalence rate at each calendar year by publication

For the US data, prevalence was found to differ in the different age categories and some publications examined restricted population age groups such as 50 years and over, 65 years and over, or 18-64 years. Therefore, to obtain an overall prevalence rate accounting for age by year and use all of the available data, the data from each publication was sorted into two age categories: individuals under 50 years and individuals 50 years and over. A regression line of best fit was then fitted to the data (Prevalence per 100,000 = intercept + slope x year) so an estimate of the prevalence rate in each age category could be extrapolated for later years. With population figures taken from latest available US census data (2018) for the two chosen age categories and the prevalence rate for each age category obtained from the regression line, it was possible to estimate the total number of IPF cases in 2018.

> "The Company was "very pleased" to receive orphan drug designation (ODD) in both the US and EU. The EMA cited clinically relevant biomarker data as a justification for the ODD designation. The data presented provided evidence of a "clinically relevant advantage" over existing treatments, offering the potential to "address a significant unmet medical need.
>
> **BioTech**, CEO

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## The Results

For the US data, the analysis determined that the:

- estimated number of people with **IPF under 50 years was 14669.24.**
- estimated number of people with **IPF 50 years and over was 110154.46.**
- estimated total number of people with **IPF in 2018 was 124,824 (95% CI: 124,131-125,5160).**
- prevalence rate for IPF in the US in 2018 was **38.2 per 100,000 (95% CI: 37.9 – 38.4).**

## The Impact

As according to the FDA an orphan disease must affect no more than 200,000 people in the total population, which was 327 167 439 in the U.S. in 2018, the prevalence of IPF must be less than 61 per 100,000 people.

- **The calculated US prevalence rate of 38.2 per 100,000 for IPF met FDA criteria for orphan disease status and consequently the investigative agent was a candidate orphan drug.**
- **Orphan drug designation was granted for the new agent in the treatment of IPF by the FDA based on this evidence.**
- **Orphan drug designation was granted by the EMA for the new agent in the treatment of IPF based on evidence generated from the EU dataset.**



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# Why Exploristics?

## Expertise In Early Development

The development of investigational drugs is a complex and expensive process with many risks. For over ten years our teams have been supporting and de-risking clinical development with their in-depth statistics and modelling expertise. Our study planning, statistical analysis and programming services add value to early stage development programmes by ensuring they deliver the robust evidence needed for incisive, informed decision-making.

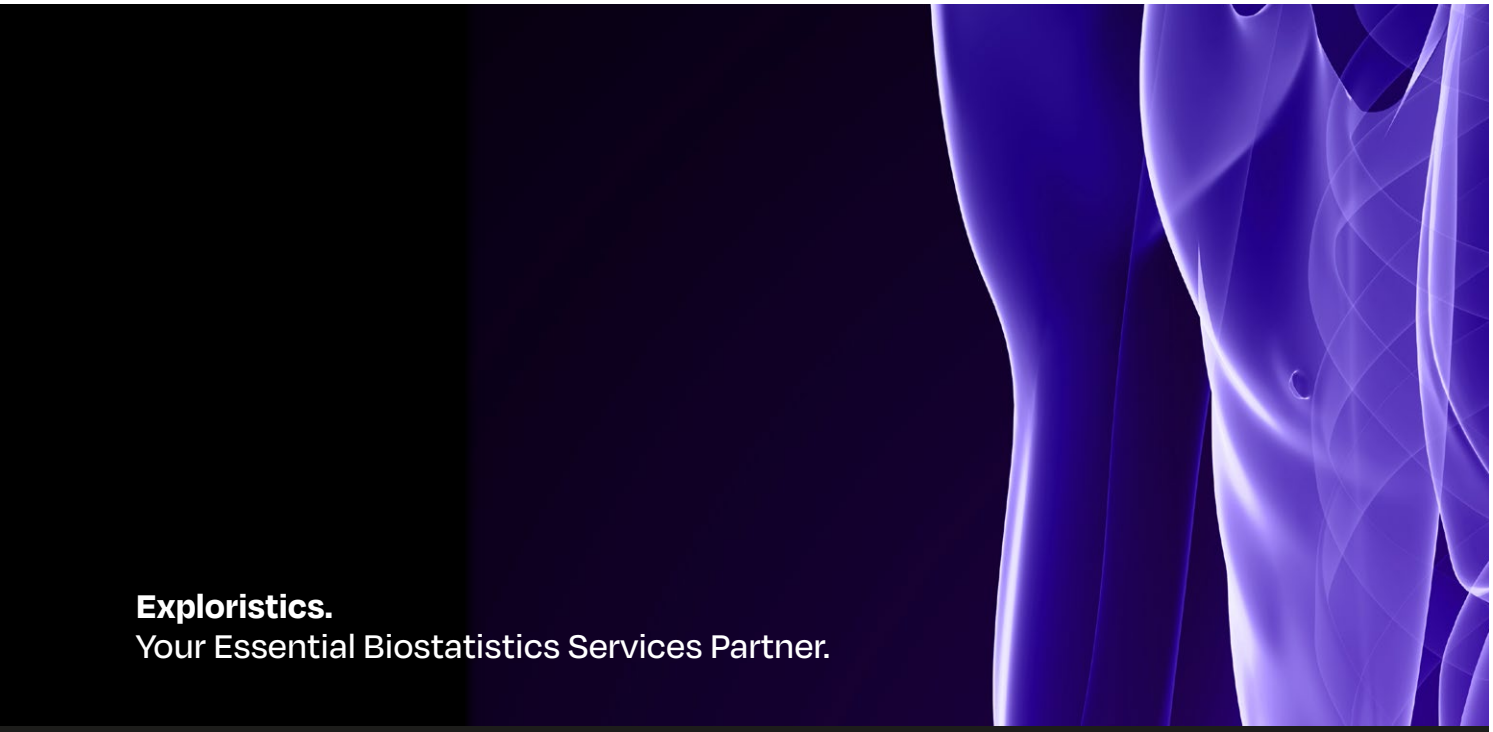
With many of our development solutions built around our unique **KerusCloud** platform, we can provide exceptional, bespoke, end-to-end biostatistics support from strategic decision-making and protocol development to analysis, reporting and stakeholder engagement.

## Robust Evidence Packages

The unique offering of our comprehensive biostatistics services in combination with **KerusCloud** ensures that Exploristics can help to generate strong evidence packages to support regulatory engagement or investment, accelerating development timelines and increasing the value of pipelines.

## Let's talk!

If you'd like to discuss this case study further or learn more on how our **technology enabled services** can support your development project, please contact our VP of Sales & Marketing, Abbas Shivji, at **abbas.shivji@exploristics.com** or **book a call**.



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Your Essential Biostatistics Services Partner.