**Dupixent – Prix Galien 2021**

**SECTION 3: BACKGROUND (300 words max)**

**Current Word Count: 300**

Allergic and atopic conditions – including asthma, atopic dermatitis, eosinophilic esophagitis, CRSwNP and food allergies – are increasing at alarming rates, with millions now suffering from severe and uncontrollable disease. Type 2 inflammation has long been associated with these conditions, suggesting they might share a common underlying immune abnormality. IL-4 was discovered in the early 1980s by groups led by Bill Paul (NIH) and Bob Coffman (DNAX Research Institute), and shown to induce type 2 markers such as immunoglobulin E;6 shortly thereafter, IL-13 was discovered and shown to share a receptor system with IL-4, as well as many biologic properties.7

These early findings led to the theory that IL-4 and IL-13 were key drivers of type 2 inflammation and associated type 2 inflammatory diseases. They also prompted efforts to treat type 2 inflammatory diseases by blocking IL-4 and IL-13, most notably by Immunex (using a soluble IL-4 receptor, Nuvance) and Amgen (using a HumAb mouse-derived antibody blocking a shared IL-4/IL-13 receptor component). Unfortunately, clinical trials using these early therapeutic candidates failed in asthma, atopic dermatitis and other allergic conditions, causing most to abandon the notion that IL-4 and IL-13 were key drivers of type 2 inflammation.

Regeneron scientists (based on their highly cited work from the 1990s) discovered new complexities in the IL-4 and IL-13 receptor system, and recognized limitations in the Amgen HumAb mouse that had precluded the generation of true blocking antibodies to the complex IL-4/IL-13 receptor. Regeneron scientists undertook a multi-year effort to generate a new HumAb mouse (termed VelocImmune®)8 that was used to develop a true blocking antibody to the shared IL-4/IL-13 receptor system, which they named dupilumab. Dupilumab provided unprecedented benefits in multiple animal models of type 2 inflammatory disease, compelling Sanofi to partner with Regeneron on a collaborative clinical trial program in type 2 inflammatory diseases.

*References*

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