Media Update

New results from rilzabrutinib phase 2 study show potential to be first advanced oral treatment for moderate-to-severe asthma

- Late-breaking data presented at ATS show that treatment with rilzabrutinib led to a numerical reduction in loss of asthma control events, improvement in symptoms and was well-tolerated with no new safety signals observed
- Results support the further development and advancement into a phase 3 program
- Rilzabrutinib is one of 12 potential blockbusters in Sanofi's robust immunology pipeline and a testament to Sanofi's ability to successfully accelerate and build a portfolio of next-generation potentially transformative treatments for immune diseases
- Rilzabrutinib is currently being studied in multiple indications, including recently reported positive results from a phase 3 study in ITP with regulatory submission in H2 2024 and positive results from a phase 2 study in CSU

Paris, May 22, 2024. Encouraging results from a phase 2 study showed that treatment with oral rilzabrutinib at both high dose and low doses led to a numerical reduction in loss of asthma control (LOAC) events (the primary endpoint) and improvements in symptoms in adult patients with uncontrolled moderate-to-severe asthma. These results were presented today as a late-breaking poster at the 2024 American Thoracic Society (ATS) International Conference in San Diego and will support the phase 3 program where a twice-daily dose of rilzabrutinib will be studied for moderate-to-severe asthma.

Asthma is one of the most common chronic respiratory diseases affecting millions of people worldwide. Despite standard-of-care treatment, about 50% of patients with asthma remain uncontrolled with a high symptom burden that impacts their quality of life.

> ***Tanya M. Laidlaw, MD***
> Director of Translational Research in Allergy Brigham and Women's Hospital, Boston, MA
> *"Many of my patients with asthma who are treated with standard of care inhaled therapies, even those with infrequent asthma attacks, still suffer from asthma symptoms and their activities are limited because of it. These patients may not qualify for a biologic medicine today but could benefit from an oral therapy that intervenes earlier in the disease. These results are encouraging as they show an improvement in asthma symptoms and a numerical reduction in Loss of Asthma Control events – important parameters in the treatment of this chronic respiratory condition that can significantly impact our patients' daily lives."*

In this proof-of-concept study, treatment with high and low dose rilzabrutinib resulted in a 36% [OR: 0.584 (0.253, 1.349)] and 25% [OR:0.570 (0.202, 1.608)] relative risk reduction in loss of asthma control (LOAC) events, respectively, at week 12 (primary endpoint). Nominally significant and clinically meaningful improvements in asthma symptoms were also observed with a -0.54/-0.59 LS mean difference in asthma control questionnaire, ACQ-5. Improvements in ACQ-5 were seen as early as week 2.

Rilzabrutinib high and low doses were well tolerated over 12 weeks of treatment with no events of cytopenia, hemorrhagic events, or atrial fibrillation and no imbalance in liver function tests. Treatment-emergent adverse events (TEAEs) occurring with higher frequency with rilzabrutinib versus placebo were diarrhea (10.9% and 9.4% with rilzabrutinib high and low dose, versus 0% and 3.1% with matching placebo, respectively).

> ***Houman Ashrafian***
> Executive Vice President, Head of Research and Development, Sanofi

"We are incredibly encouraged by the reduction in loss of asthma control events and improvements in asthma symptoms and look forward to advancing rilzabrutinib into a broader phase 3 clinical development program to further explore its potential in this disease. Advanced oral therapies have the potential to change the treatment paradigm for diseases like asthma, and we remain committed to exploring disruptive mechanisms of action for people living with uncontrolled chronic inflammatory diseases."

Rilzabrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

About the study

This phase 2 study is a randomized, double-blind, placebo-controlled, parallel-group, 12-week proof-of-concept study to assess the efficacy, safety, and tolerability of rilzabrutinib in participants with moderate-to-severe asthma who are not well controlled on inhaled corticosteroid (ICS) plus long-acting β2 adrenergic agonist (LABA) therapy. Two doses of rilzabrutinib, 800 mg daily and 1200 mg daily, were studied. Patients were randomized 1:1 to receive either rilzabrutinib or placebo to be added to a background therapy of ICS/LABA which was withdrawn during the 12-week treatment period.

The primary endpoint was reduction in LOAC events. Secondary endpoints included asthma control (measured by the asthma control questionnaire, ACQ-5) and asthma quality of life (measured by the asthma quality of life questionnaire, AQLQ) or lung function (measured by FEV1).

About rilzabrutinib

Rilzabrutinib is an oral, reversible, covalent BTK inhibitor that has the potential to be a first- and/or best-in-class treatment for several immune-mediated diseases. BTK, expressed in B cells and mast cells, plays a critical role in multiple immune-mediated disease processes. With the application of Sanofi's TAILORED COVALENCY® technology, rilzabrutinib can selectively inhibit the BTK target while potentially reducing the risk of off-target side effects.

Rilzabrutinib is being studied across a variety of immune-mediated diseases, including immune thrombocytopenia (ITP), asthma, chronic spontaneous urticaria, prurigo nodularis, IgG4-related disease, and warm autoimmune hemolytic anemia.

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across the world, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.
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