AB2 Bio announces readiness for recruitment in pivotal Phase 3 trial of Tadekinig alfa, a novel human recombinant interleukin-18 binding protein, in children with genetic diagnosis of NLRC4-MAS mutation or XIAP deficiency, with amended design in the U.S. and Canada

Lausanne (Switzerland), March 21, 2019 — AB2 Bio Ltd, a Swiss advanced clinical-stage biotech company, specialized in developing innovative therapies for the treatment of severe systemic autoinflammatory diseases, announced today that a single-arm open label design with a randomized withdrawal phase for its ongoing pivotal Phase 3 trial under an Investigational New Drug (IND) Application for its product candidate Tadekinig alfa, has been accepted by the U.S. Food and Drug Administration (FDA). Tadekinig alfa is a recombinant human interleukin-18 binding protein targeting the treatment of dysregulated and persistent IL-18-mediated inflammatory processes which are the basis of autoinflammatory and autoimmune diseases, such as NLRC4-MAS, XIAP deficiency, systemic Juvenile Idiopathic Arthritis, and Adult onset Still's Disease.

“We are delighted about the FDA’s acceptance and look forward to continuing our pivotal Phase 3 clinical trial under the amended protocol, which will now give all patients the chance to be initially treated with Tadekinig alfa rather than having only a 50% chance as in the previous version of the protocol,” says Eduardo Schiffrin, M.D., AB2 Bio’s Medical Director. “So far there is no approved therapy for autoinflammatory diseases associated with high free IL-18 levels. As a result, there is a high unmet medical need among patients suffering from these severe and life-threatening conditions. By testing a potentially effective new therapy, we hope to improve their prospects and quality of life.”

AB2 Bio is currently enrolling patients in the U.S. and Canada. The clinical trial details including trial locations can be found under ClinicalTrials.gov Identifier: NCT03113760.

About the Pivotal Phase 3 Trial in Patients with Monogenic, Interleukin-18 Driven Autoinflammation due to NLRC4-MAS Mutation or XIAP Deficiency

Recently, single point mutations in the NLRC4 gene have been identified. These genetic, gain of function mutations give rise to severe, life-threatening systemic inflammation associated with extremely high levels of IL-18, the therapeutic target of Tadekinig alfa. AB2 Bio is conducting a pivotal Phase 3 clinical trial with its experimental drug Tadekinig alfa in patients with NLRC4 mutations and patients carrying mutations of the X-linked inhibitor of apoptosis protein (XIAP). NLRC4 mutations and XIAP deficiency are part of primary Hemophagocytic Lymphohistiocytosis (HLH).

About Hemophagocytic Lymphohistiocytosis (HLH)

HLH is a potentially life-threatening condition characterized by severe systemic inflammation that, if left untreated, may rapidly evolve into multiple-organ failure and death. Children with HLH usually develop symptoms within the first months or years of life which may include fever, pancytopenia, coagulopathy, and hemophagocytosis. These disorders can be either inherited (genetic or primary) or secondary to other conditions such as rheumatic conditions, cancer or infections. In the case of rheumatic HLH or Macrophage Activation Syndrome (MAS) the underlying pathogenic process involves a "cytokine storm" produced by highly activated lymphocytes and macrophages. A key aspect of Tadekinig alfa's therapeutic profile is that it interferes with the immunodominant mediator, free IL-18.

About Tadekinig alfa, a Recombinant Human Interleukin-18 Binding Protein

Tadekinig alfa is a recombinant interleukin-18 binding protein (r-hIL-18BP), that binds with high affinity to IL-18, a major inflammatory mediator. It is administered subcutaneously. In healthy people, IL-18 and IL-18BP are present constitutively in blood with a large excess of IL-18BP keeping levels of free IL-18 undetectable. However, in patients with inflammatory diseases, the IL-18/IL-18BP balance is disrupted, resulting in high levels of free and active IL-18, which leads to pathological inflammation. While the time-limited inflammatory response is a natural defense mechanism intended to clear pathogens and limit harm to the body, dysregulated and persistent inflammatory processes are the basis of several chronic inflammatory and autoimmune diseases. Administration of Tadekinig alfa restores the IL-18/IL-18BP balance, by removing free IL-18 and thereby reducing inflammation.

Excellent safety and tolerability of Tadekinig alfa have been demonstrated in human subjects in Phase 1/1b clinical trials and a Phase 2 trial. Early signs of efficacy of Tadekinig alfa have been shown in a Phase 2 trial in patients suffering from refractory Adult onset Still's disease, as well in single compassionate use cases in NLRC4-MAS, XIAP, and Systemic onset Juvenile Idiopathic Arthritis.

About Regulatory Designations Granted to Tadekinig alfa

Tadekinig alfa has been granted Orphan Drug Designation by the FDA for the treatment of HLH and Still's disease, including Adult-onset Still's Disease and systemic Juvenile Idiopathic Arthritis, and by EMA for the treatment of HLH. In addition, the FDA has granted Breakthrough Therapy Designation for the treatment of monogenic, IL-18 associated

autoinflammatory conditions with ongoing systemic inflammation, and Pediatric Rare Disease Designation for the treatment of primary HLH.

About Free IL-18 Assay, a Key to Precision Medicine

AB2 Bio has developed a proprietary assay detecting free IL-18 thereby allowing the identification of indications that are associated with and driven by free IL-18. Patients with high levels of free IL-18 can be identified in order to maximize the clinical impact of treatment with Tadekinig alfa. Patients unlikely to respond to Tadekinig alfa will not be unnecessarily exposed to a potentially ineffective treatment.

About AB2 Bio

AB2 Bio Ltd is a private advanced clinical-stage biotech company located in the Innovation Park at the Ecole polytechnique fédérale de Lausanne (EPFL), Switzerland. AB2 Bio is fully dedicated to the development of treatments against autoinflammatory diseases.
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