



Kymera Therapeutics to Present Preclinical Data on its First-in-Class Selective and Potent Oral IRAK4 Degraders in Cutaneous Inflammation

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Company names first inflammation/immunology disease indication: Hidradenitis suppurativa

Cambridge, Mass. (February 5, 2020) – Kymera Therapeutics Inc., a biotechnology company pioneering targeted protein degradation to discover breakthrough medicines for patients, today announced the company will present preclinical data demonstrating that oral daily dosing of its IRAK4 degraders completely suppressed IRAK4 protein expression in skin and immune cells and inhibited cutaneous inflammation. Data support the development of Kymera's degraders for chronic inflammatory and autoimmune diseases, including the company's first named inflammation/immunology disease indication, hidradenitis suppurativa (HS). Research will be presented at the 9th European Hidradenitis Suppurativa Foundation Scientific Conference in Athens, Greece on Feb. 6 at 10:30 AM GMT+2 in the Ilissos room of the Athens Caravel hotel (Abstract #86).

IRAK4 is a protein known to play a significant role in inflammation mediated by the activation of toll-like receptors (TLRs) and IL-1 receptors (IL-1Rs). While TLR and IL-1R signaling via IRAK4 is involved in the normal immune response, aberrant activation of those pathways is the underlying cause of multiple inflammatory and autoimmune conditions, including HS, atopic dermatitis and rheumatoid arthritis.

"Our latest findings build on the data presented last year at the American College of Rheumatology (ACR) showing the ability of IRAK4 knockdown in skin and spleen to suppress cutaneous inflammation in mice," said Jared Gollob, MD, CMO of Kymera Therapeutics. "Importantly, we have also demonstrated that oral daily administration of an IRAK4 degrader leads to complete knockdown of IRAK4 in skin and immune cells in higher species that is well-tolerated. These findings support development in hidradenitis suppurativa, a chronic inflammatory skin disease where robust IRAK4 inhibition has the potential to block the painful, destructive neutrophilic and lymphocytic inflammation driven by chronic TLR and IL-1R activation."

Last November, at the ACR meeting in Atlanta, Kymera introduced its selective and potent oral IRAK4 degraders, showing *in vitro* inhibition of cytokine and chemokine induction by TLR agonists and IL-1 β that was superior to IRAK4 kinase inhibitors as well as suppression of neutrophil infiltration and IL-1 β production *in vivo* in the mouse MSU air pouch model.

"Inhibition of the TLR/IL-1R pathway with a single oral small molecule targeted against IRAK4 has great potential for the treatment of devastating autoimmune and chronic inflammatory diseases like HS, where inflammation is caused by multiple different IL-1 family cytokines as well as TLR stimulation," said Nello Mainolfi, PhD, co-founder, President and CEO, Kymera Therapeutics. "It is encouraging to see that we can safely achieve the level of IRAK4 knockdown in relevant tissue necessary to treat a disease like HS which has a high inflammatory burden. We look forward to moving our lead compound into the clinic in healthy volunteers by the end of 2020."

EHSF Study Highlights

ABSTRACT #86, "Identification of highly potent and selective Interleukin-1 receptor associated kinase 4 (IRAK4) degraders for the treatment of hidradenitis suppurativa," will be presented by Veronica Campbell, Principal Scientist at Kymera Therapeutics.

New data showed:

- Kymera's oral IRAK4 degrader lowered IRAK4 levels in the skin and spleen in a preclinical model of cutaneous inflammation and reduced skin thickening as well as circulating Th1 and Th17 cytokines (including IL-1 β , IL-6 and IL-17) to the same extent as topical corticosteroids.
- Oral daily dosing of an IRAK4 degrader in higher species for 2 weeks led to complete suppression of IRAK4 in skin, lymph nodes and peripheral blood mononuclear cells and was safe and well-tolerated.

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About Kymera Therapeutics

Kymera Therapeutics is a biotechnology company pioneering a transformative new approach to treating previously untreatable diseases. The company is advancing the field of targeted protein degradation, accessing the body's innate protein recycling machinery to degrade dysregulated, disease-causing proteins. Powered by Pegasus™, a game-changing integrated degradation platform, Kymera is accelerating drug discovery with an unmatched ability to target and degrade the most intractable of proteins, and advance new treatment options for patients. For more information visit, www.kymeratx.com.

About Pegasus™

Pegasus™ is Kymera Therapeutics' proprietary protein degradation platform, created by its team of experienced drug hunters to improve the effectiveness of targeted protein degradation and generate a pipeline of novel therapeutics for previously undruggable diseases. The platform consists of informatics driven target identification, novel E3 ligases, proprietary ternary complex predictive modeling capabilities, and degradation tools.