Kiniksa Pharmaceuticals Logo

Kiniksa Presents Preclinical Data on the Role of GM-CSF in GCA at the 2019 ACR/ARP Annual Meeting

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- Mavrilimumab suppresses pathogenic immune responses in a validated in vivo model of medium and large vessel vasculitis -

- Additional human ex vivo data support rationale for targeting GM-CSF in GCA -

HAMILTON, Bermuda, Nov. 12, 2019 (GLOBE NEWSWIRE) -- Kiniksa Pharmaceuticals, Ltd. (Nasdaq: KNSA) ("Kiniksa"), a biopharmaceutical company focused on discovering, acquiring, developing and commercializing therapeutic medicines for patients with significant unmet medical need, today announced that it presented preclinical data on the role of granulocyte macrophage colony stimulating factor (GM-CSF) in giant cell arteritis (GCA) at the 2019 American College of Rheumatology/Association of Rheumatology Professionals (ACR/ARP) Annual Meeting.

"The data presented at ACR/ARP further support the mechanistic rationale of targeting GM-CSFRα in patients with GCA," said Sanj K. Patel, Chief Executive Officer and Chairman of the Board of Kiniksa. "Notably, GM-CSF has a role as an inflammatory cytokine in medium and large vessel vasculitis, and the density of inflammatory cells in inflamed vessels appears to be GM-CSF-dependent. Additionally, mavrilimumab significantly reduced arterial inflammation in a validated *in vivo* model of vasculitis. We continue to advance our global Phase 2 clinical trial of mavrilimumab in GCA and expect top-line data in the second half of 2020."

Dr. Cornelia M. Weyand[1] and Dr. Maria C. Cid[2] presented preclinical data sponsored by Kiniksa, which support the mechanistic rationale for targeting granulocyte macrophage colony stimulating factor receptor alpha (GM-CSFRα) in patients with GCA.

Dr. Cornelia M. Weyand presented ***GM-CSF is a Pro-Inflammatory Cytokine in Experimental Vasculitis of Medium and Large Arteries***.

- Data from this validated *in vivo* model of vasculitis showed that, compared to treatment controls, mavrilimumab, a monoclonal antibody inhibitor targeting GM-CSFRα, reduced tissue inflammation in the arteries.
- In the model, normal human arteries were engrafted into immune-deficient mice. Following the engraftment, peripheral blood mononuclear cells from patients with GCA were transferred to the mice which then caused vasculitis to appear in the normal arteries within 7-10 days.
- After the inflammation had been established, animals were treated with mavrilimumab. Mavrilimumab demonstrated statistically significant reductions in the number of CD3+ T-cells and in innate and adaptive immune responses in the inflamed arteries in addition to significant reductions in key cytokines known to play a role in GCA pathology including interferon-gamma (IFN-γ). These data illustrate that blockade of GM-CSFRα signaling had a strong anti-inflammatory treatment effect.
- The reduced expression of IFN-γ in mice treated with mavrilimumab is of significance for treating GCA as it is the signature cytokine produced by the T helper type 1 (T_H1) cell lineage which, along with GM-CSF, has been implicated in multinucleated giant cell formation. The T_H1 signature is relatively unresponsive to glucocorticoid therapy and often persists in steroid-treated patients, and is believed to mediate chronic and refractory disease.

Dr. Maria C. Cid presented ***GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients with Giant Cell Arteritis***.

- Data from this study examining human temporal artery biopsies from two independent sources showed the GM-CSF signaling pathway molecular signature was upregulated in GCA biopsies versus control at both the messenger ribonucleic acid (mRNA) and protein level.
- GM-CSF and T_H1 pathway signatures (including IFN-γ) were demonstrated in GCA patient temporal arteries by independent analytical techniques. The data also demonstrated active GM-CSF signaling in diseased tissue is evidenced by increased expression of PU.1, a transcription factor downstream of GM-CSF signaling, in the vessel wall.
- Additionally, treatment of *ex vivo* cultures of GCA arteries with mavrilimumab suppressed expression of these gene products, indicating the biological effect of mavrilimumab on genes relevant to GCA pathophysiology.

Kiniksa is developing mavrilimumab, an investigational fully-human monoclonal antibody that is designed to antagonize GM-CSF signaling by binding to the alpha subunit of the GM-CSF receptor, for the potential treatment of GCA.

GCA is a chronic inflammatory disease of medium-large arteries that causes headaches, jaw and other muscle claudication as well as ischemic visual loss and blindness. Kiniksa estimates U.S. prevalence of approximately 75,000 to 150,000 patients with similar prevalence rates for other major markets.

Kiniksa is enrolling a randomized, double-blind, placebo-controlled, global Phase 2 proof-of-concept clinical trial of mavrilimumab in subjects with GCA in fifteen countries. The primary efficacy endpoint involves measuring GCA flares during the 26-week treatment period. Top-line data are expected in

the second half of 2020.

The materials for the presentations are available through the Science section of Kiniksa's website (www.kiniksa.com).

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About Mavrilimumab
Mavrilimumab is an investigational fully-human monoclonal antibody that is designed to antagonize GM-CSF signaling by binding to the alpha subunit of the GM-CSF receptor. Kiniksa's lead indication for mavrilimumab is GCA, a chronic inflammatory disease of medium-large arteries.

About Kiniksa
Kiniksa is a biopharmaceutical company focused on discovering, acquiring, developing and commercializing therapeutic medicines for patients suffering from debilitating diseases with significant unmet medical need. Kiniksa has a pipeline of product candidates across various stages of development, focused on autoinflammatory and autoimmune conditions. For more information, please visit www.kiniksa.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, statements regarding: our development of mavrilimumab for the potential treatment of GCA; our conclusions from pre-clinical data for mavrilimumab; our expected timing of topline data from our Phase 2 clinical trial of mavrilimumab in GCA; and our estimates of GCA prevalence in the United States and other major markets.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including without limitation, the following: potential delays or difficulty in enrollment of patients in, and activation of sites for, our clinical trials; potential complications in coordinating among requirements, regulations and guidelines of regulatory authorities across a number of jurisdictions for our global clinical trials; potential amendments to our clinical trial protocols initiated by us or required by regulatory authorities; potential delays or difficulty in completing our clinical trials, including as a result of our clinical trial design; potential undesirable side effects caused by our product candidates; our potential inability to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities or otherwise producing negative, inconclusive or commercially uncompetitive results; potential for changes between final data and any preliminary and interim "top-line" data we announce; impact of additional data from us or other companies; our potential inability to replicate in later pre-clinical and clinical trials positive results from our earlier pre-clinical and clinical trials; drug substance and/or drug product shortages caused by issues at our third-party manufacturers' facilities; our reliance on certain third parties as the sole source of supply of the drug substance and drug products used in our product candidates; our reliance on third parties to conduct our research, pre-clinical studies, clinical trials, and other trials for our product candidates; changes in our operating plan; and our ability to attract and retain qualified personnel.

These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission ("SEC") on November 5, 2019, and our other reports filed with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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