Kiniksa Announces Positive Results for Mavrilimumab Phase 2 Trial in Non-Mechanically Ventilated Severe COVID-19 Patients

April 12, 2021

– Primary endpoint achieved: the proportion of patients alive and free of mechanical ventilation at Day 29 was 12.3 percentage points higher with mavrilimumab versus placebo (p=0.1224 met predefined statistical threshold of p<0.2) –
– 65% reduction in risk of mechanical ventilation/death with mavrilimumab versus placebo (p=0.0175) –
– 61% reduction in risk of death with mavrilimumab versus placebo (p=0.0726) –
– Clinical improvement was observed on top of steroids and/or antivirals –
– Enrollment in the Phase 3 portion of the trial ongoing –

HAMILTON, Bermuda, April 12, 2021 (GLOBE NEWSWIRE) -- Kiniksa Pharmaceuticals, Ltd. (Nasdaq: KNSA) ("Kiniksa"), a biopharmaceutical company with a portfolio of assets designed to modulate immunological pathways across a spectrum of diseases, today announced the Phase 2 portion of the Phase 2/3 trial of mavrilimumab in non-mechanically-ventilated patients (Cohort 1) with severe COVID-19 pneumonia and hyperinflammation achieved its primary efficacy endpoint of the proportion of patients alive and free of mechanical ventilation at Day 29. Mavrilimumab is an investigational fully-human monoclonal antibody that targets granulocyte macrophage colony stimulating factor receptor alpha (GM-CSFRα).

"These data suggest that mavrilimumab may be a transformational treatment option for patients with severe pneumonia due to hyper-inflammatory syndromes, including COVID-19," said Sanj K. Patel, Chief Executive Officer and Chairman of the Board of Kiniksa. "Additionally, they reinforce our belief in the potential broad utility of mavrilimumab, which has demonstrated positive clinical data across three indications: giant cell arteritis, rheumatoid arthritis, and severe COVID-19. We are engaged with various government agencies to potentially secure resources to help bring mavrilimumab to patients as soon as possible."

The Phase 2/3 trial is a global, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of mavrilimumab treatment in adults hospitalized with severe COVID-19 pneumonia and hyperinflammation.

In the Phase 2 portion of the trial, patients were enrolled into 2 cohorts: non-mechanically ventilated patients (Cohort 1) requiring supplemental oxygen to maintain SpO2 ≥ 92%; and mechanically ventilated patients (Cohort 2) for whom mechanical ventilation was initiated within 48 hours prior to randomization. There was a seamless transition in the enrollment of patients in both cohorts from the Phase 2 into the Phase 3 portions of the trial.

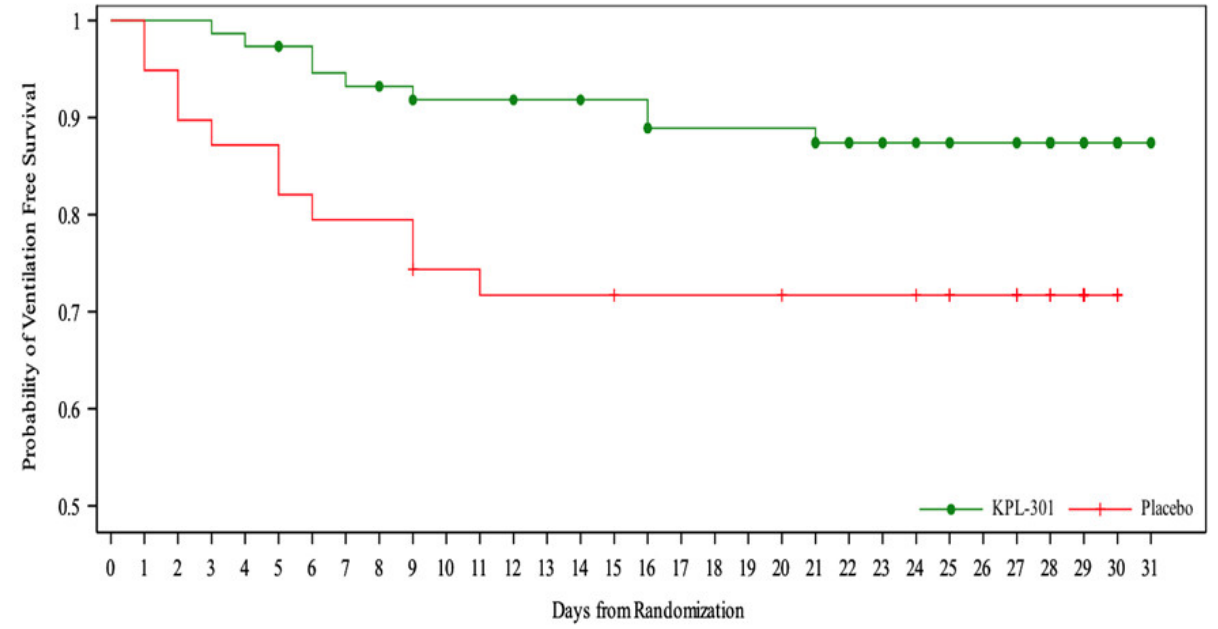
In the non-mechanically ventilated cohort (Cohort 1), 116 patients with hypoxia and severe COVID-19 pneumonia/hyperinflammation were enrolled across sites in the United States, Brazil, Chile, Peru, and South Africa. Patients were randomized in a 1:1:1 ratio to receive a single intravenous (IV) dose of mavrilimumab 10 mg/kg, 6 mg/kg, or placebo. The primary efficacy endpoint was the proportion of patients alive and free of mechanical ventilation at Day 29. Key secondary endpoints included Time to Two-Point clinical improvement on the National Institute of Allergy and Infectious Diseases (NIAID) scale, Time to Return to Room Air, and Mortality at Day 29. The prespecified evidentiary standard for Phase 2 endpoints was a 2-sided alpha value of 0.2, without adjustment for multiplicity.

Baseline demographics were balanced across treatment arms: the population was ethnically/racially diverse (43% non-white), 49% were obese (body mass index ≥ 30), and 29% were older than 65 years. All patients received local standard of care therapy: 96% received corticosteroids/dexamethasone and 29% received antivirals/remdesivir.

Non-mechanically ventilated patients (Cohort 1) treated with mavrilimumab demonstrated a reduction in mechanical ventilation and death at Day 29 pooled across dose levels.

- The proportion of patients alive and free of mechanical ventilation at Day 29 was 12.3 percentage points higher in mavrilimumab recipients (86.7%) compared to placebo recipients (74.4%) (Primary efficacy endpoint; p=0.1224).
    - Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death through Day 29 (Hazard Ratio (HR) = 0.35; p=0.0175).

A Media Snippet accompanying this announcement is available by clicking on the image or link below:



KPL-301	75	75	75	75	74	73	71	69	68	67	65	65	65	64	64	63	63	59	59	59	59	59	55	52	50	49	47	47	45	38	18	3
Placebo	39	39	37	35	34	34	32	31	31	31	28	28	27	27	27	27	26	26	26	26	26	25	25	25	25	24	22	22	17	14	4	

Note: Time to ventilation or death by Day 29 is defined as time (in days) from randomization to the date of death or start date of using mechanical ventilation (NIAID <= 2) by Day 29. All subjects who never had NIAID <= 2 by Day 29 will be censored at last assessment date of NIAID 8-point ordinal scale.

- Day 29 mortality was 12.5 percentage points lower in mavrilimumab recipients (8%) compared to placebo recipients (20.5%) (p=0.0718).
    - Mavrilimumab recipients experienced a 61% reduction in the risk of death through Day 29 (HR= 0.39; p=0.0726).
- No apparent differences were observed between the 10 mg/kg and 6mg/kg IV treatment arms.

Mavrilimumab was well-tolerated and exhibited a favorable safety profile.

- One treatment-emergent serious adverse event related to study drug was reported on placebo, and there were no notable dose-related adverse events. Infections were noted in all groups including placebo recipients. All thrombotic events occurred in placebo recipients.

“The results from the Phase 2 portion of the Phase 2/3 trial of mavrilimumab in non-mechanically-ventilated patients with severe COVID-19 signify a potential additive treatment effect of mavrilimumab on top of corticosteroids in reducing mechanical ventilation and death in a diverse population,” said John F. Paolini, MD, PhD, Chief Medical Officer of Kiniksa. “In the context of other treatments being evaluated, we are particularly encouraged by the benefit/risk of GM-CSF receptor inhibition with mavrilimumab given not only the sustained treatment effect demonstrated throughout the 29-day observation period after a single infusion but also the well-tolerated safety profile to-date.”

Despite encouraging progress in the vaccine rollout and in recent data from early-use therapeutics, hospitalized COVID-19 patients requiring supplemental oxygen are at high risk for progression to mechanical ventilation and death even when treated with the current standard of care, including dexamethasone and antivirals. Additionally, the emergence of potentially vaccine-resistant variants as well as the uncharacterized duration of vaccine protection highlight the uncertain course of the pandemic. Beyond vaccines and therapeutics, there are public health challenges related to both access to care and willingness to be vaccinated. Data from the Centers of Disease Control and Prevention (CDC) indicate that these challenges are heightened among minority populations, which are well-represented in the mavrilimumab Phase 2/3 trial in severe COVID-19 pneumonia and hyperinflammation.

“Mavrilimumab is a potentially transformational treatment option for people with COVID-19 infection who require hospitalization and supplemental oxygen therapy,” said Bruce Trapnell, MD, Professor of Medicine and Pediatrics at the University of Cincinnati. “While vaccines are important in preventing COVID-19 infection, there is an urgent unmet public health need for therapeutics to combat hyperinflammation in people with active infection. GM-CSF, a cytokine critical to normal function of the lungs, is central to the pathogenesis of COVID lung infection, and inhibition of its receptor with mavrilimumab is emerging as a promising potential treatment option.”

Kiniksa is engaged with the U.S. Food and Drug Administration (FDA) and other government agencies to identify pathways, including potential Emergency Use Authorization, for accelerated availability of mavrilimumab as a therapeutic option for severe COVID-19 patients.

Kiniksa has completed enrollment of the Phase 2 portion of the Phase 2/3 clinical trial in severe COVID-19 pneumonia and hyperinflammation. The company continues to enroll patients in the Phase 3 portion of the clinical trial, which has already enrolled over 250 patients. The company expects to provide next steps for the broader mavrilimumab development program this quarter.

About Mavrilimumab
Mavrilimumab is an investigational fully-human monoclonal antibody that blocks activity of GM-CSF by specifically binding to the alpha subunit of the GM-CSF receptor. Mavrilimumab was dosed in over 550 patients with rheumatoid arthritis through Phase 2b clinical studies in Europe and achieved prospectively-defined primary endpoints of efficacy and safety. Kiniksa’s lead indication for mavrilimumab is giant cell arteritis (GCA), a rare inflammatory disease of medium-to-large arteries. A Phase 2 trial in GCA achieved both the primary and secondary efficacy endpoints with statistical significance. Kiniksa is also evaluating mavrilimumab in severe COVID-19 pneumonia and hyperinflammation. The FDA granted Orphan Drug designation to mavrilimumab for the treatment of GCA in 2020.

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’s portfolio of assets, ARCALYST, mavrilimumab, vixarelimab and KPL-404, are based on strong biologic rationale or validated mechanisms, target underserved conditions and offer the potential for differentiation. These assets are designed to modulate immunological pathways across a spectrum of diseases. For more information, please visit www.kiniksa.com.

Forward-Looking Statements

The information contained in 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 beliefs that the data suggest that mavrilimumab has the potential to be a transformational treatment option for hospitalized patients with severe pneumonia due to hyper-inflammatory syndromes, including COVID-19, requiring supplemental oxygen; our belief that the inhibition of the GM-CSF receptor with mavrilimumab has the potential to be a promising treatment option; our beliefs that the data signify a potential additive treatment effect of mavrilimumab on top of corticosteroids in the context of standard of care treatment in reducing mechanical ventilation and death in a diverse population; our belief that, even as vaccines are important in preventing COVID-19 infection, there is an urgent unmet public health need for therapeutics to combat hyperinflammation in people with infection; our effort to secure governmental resources to potentially bring mavrilimumab to patients as soon as possible; our belief in the potential broad utility of mavrilimumab, which has demonstrated positive clinical data across three indications: giant cell arteritis, rheumatoid arthritis, and severe COVID-19; timing to provide next steps for the broader mavrilimumab development program; and the potential for all of our clinical stage product candidates to offer differentiation.

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: the impact of additional data from us, or other companies; the potential inability to replicate in later clinical trials encouraging or positive results from earlier studies for mavrilimumab in severe COVID-19 pneumonia and hyperinflammation in later clinical trials; the evolving standard of care for the treatment of patients who develop severe COVID-19 pneumonia and hyperinflammation; the potential for undesirable side effects to be caused by mavrilimumab; changes to our clinical trial protocol; case rates of severe COVID-19 pneumonia and hyperinflammation in various geographies; our reliance on third parties to manufacture our product candidates and conduct our clinical trials; meetings with the Food and Drug Administration and other government agencies to secure resources to bring mavrilimumab to patients; the potential impact of the COVID-19 pandemic and measures taken in response to the pandemic; changes in our operating plan and funding requirements; existing or new competition; and our ability to attract and retain qualified personnel.

These and other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (“SEC”) on February 25, 2021 and our other reports subsequently filed with or furnished to 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.

Every Second Counts!™

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