From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Mon, 27 Apr 2020 00:42:34 +0000
To: Lerner, Andrea (NIH/NIAID) [E]
Subject: FW: Update: Inhibit cytokine storm in COVID-19 patients by Proteasome Inhibitors
Attachments: (b) (4)

Please respond to this person. Thanks.

From: Kircheis Dr. Ralf <RKircheis@syntacoll.de>
Sent: Wednesday, April 22, 2020 9:41 AM
To: Coomes, Stephanie (NIH/NIAID) [E] (b) (6)>; Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Cc: (b) (6); Kircheis Dr. Ralf <RKircheis@syntacoll.de>
Subject: Update: Inhibit cytokine storm in COVID-19 patients by Proteasome Inhibitors
Importance: High

Dear Dr. Fauci,
dear Dr. Coomes,

thank you for your reply from 13. April with the notice that the information has been shared with NIAID's COVID-19 research team.

Has the project already been initially evaluated by the team?

Are there any questions or need for additional information?

- I have summed up the relevant data regarding the use of proteasome inhibitors for treatment of COVID-19 patients with acute lung and systemic organ failure in a position paper, please find a Preview draft attached.

- With regard to currently ongoing trials with monoclonal antibodies against the IL-6 receptor, i.e. tocilizumab or sarilumab: These approaches go into the same direction as the present suggestion, however, inhibition of NF-κB by proteasome inhibitors could provide the unique potential to inhibit the release of multiple cytokines simultaneously, in particular strongly pro-inflammatory cytokines including IL-1, IL-6, TNFα and chemokines, such as MIP-1 and CXCL1.

- This simultaneous inhibition of multiple cytokines/chemokine seems to be advantegeaus compared to single target approaches (as with the mAb) to compensate for redundant and synergistic effects of multiple cytokines released during highly pathogenic CoV or H5N1 infection.

Looking forward to hearing from you.

Kind regards,

Ralf