Nimbus Therapeutics Publishes Structural Analysis Highlighting Mechanisms for Selective Inhibition of CTPS1

CAMBRIDGE, Mass. – September 30, 2021 – Nimbus Therapeutics, a biotechnology company designing breakthrough medicines through structure-based drug discovery and development, today published research in the *Proceedings of the National Academy of Sciences* describing the structural basis for isoform-specific inhibition of human CTPS1 (CTP synthase 1). Selective inhibition of CTPS1 is a promising approach for the treatment of autoimmune and other T cell-driven diseases, but little is known about the mechanisms underlying selective versus non-selective inhibition.

Nimbus scientists, in partnership with researchers from the University of Washington and Schrödinger, used cryo-electron microscopy (cryo-EM) to characterize the activity of CTPS inhibitors in binding to, inhibiting and distinguishing between CTPS1 and its isoform CTPS2. The cryo-EM research was funded by Nimbus and led by professor Justin Kollman at the University of Washington.

"We're proud to have conducted this impactful research in partnership with our valued colleagues at University of Washington and Schrödinger, further building on Nimbus' long history of fruitful academic collaborations," said Peter Tummino, Ph.D., Chief Scientific Officer at Nimbus. "The insights we have published will be instrumental in our efforts to develop selective inhibitors of CTPS1 that can potentially offer a powerful new means of treating autoimmune diseases and T cell-driven cancers."

"A defining feature of Nimbus' structure-based drug discovery approach is our use of leading-edge computational technology, including cryo-EM, to characterize drug targets in unprecedented detail," said Scott Edmondson, Ph.D., Senior Vice President and Head of Chemistry at Nimbus. "The discoveries made in this research, together with Nimbus' expertise in computational chemistry, molecular sciences and disease biology, will inform our ongoing development of highly selective small-molecule CTPS1 inhibitors."

The paper, entitled "Structural basis for isoform-specific inhibition of human CTPS1," published online in the *Proceedings of the National Academy of Sciences* this week: https://www.pnas.org/content/118/40/e2107968118.

About Nimbus Therapeutics

Nimbus Therapeutics designs breakthrough medicines. Utilizing its powerful structure-based drug discovery engine, Nimbus designs potent and selective small molecule compounds targeting proteins that are known to be fundamental drivers of pathology in highly prevalent human diseases and which have proven difficult for other drug makers to tackle. Nimbus is headquartered in Cambridge, Mass. www.nimbustx.com

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