



## **Nimbus Therapeutics Announces Expansion of its Drug Discovery Pipeline Across Oncology, Immunology and Metabolism**

*- AMPK $\beta$ 2, CTPS1, Cbl-b and WRN are highly promising targets for Nimbus' structure-based drug discovery approach -*

**CAMBRIDGE, Mass. – June 8, 2020 – [Nimbus Therapeutics](#)**, a biotechnology company designing breakthrough medicines through structure-based drug discovery and development, announced the expansion of the company's pipeline of small molecule candidates across a range of highly prevalent human diseases. These preclinical programs — AMPK $\beta$ 2 (AMP-activated protein kinase,  $\beta$ 2 subunit), CTPS1 (CTP synthase 1), Cbl-b (Cbl proto-oncogene B), and WRN (Werner syndrome ATP-dependent helicase) — represent promising targets across oncology, immunology and metabolism, for which Nimbus' structure-based discovery approaches are uniquely suited.

“The additional programs we're unveiling today are a testament to Nimbus' exceptional talent, the unwavering support of our investors, and the dynamic scientific collaborations we have built over the past decade,” said Jeb Keiper, M.S., MBA, Chief Executive Officer of Nimbus. “Our prolific pipeline reflects the breadth of potential we see for our discovery engine going forward, and a new chapter in Nimbus' leadership of structure-based drug discovery. We look forward to progressing these programs forward to the clinic within our development organization, which advanced our ACC inhibitor to an early proof of mechanism and is currently progressing our Tyk2 inhibitor toward Phase II.”

“With the addition of these targets, we've built a pipeline of promising therapeutics for the treatment of patients with diseases that have limited or no therapeutic options,” said Peter Tummino, Ph.D., Chief Scientific Officer of Nimbus. “Each of these targets represents the 'sweet spot' for Nimbus' approach — they are known to be fundamental drivers of highly prevalent diseases but have proven difficult for the industry to drug. As we have demonstrated with our progress on HPK1, which is being presented at AACR this month, we believe our structure-based drug discovery engine can generate the potent, selective small molecule therapeutics needed to move the needle on these targets.”

A brief overview of our newly disclosed programs follows:

- **AMPK $\beta$ 2 for cellular metabolic regulation**  
AMPK is a kinase that serves as a critical regulator of energy-sensing and metabolic homeostasis in many tissues. Small molecule activation of AMPK has long been recognized as a potential strategy to treat multiple metabolic disorders and other pathologies. Nimbus' approach leverages new understandings in AMPK subunit structure to identify activators selective for the AMPK $\beta$ 2 subtype of the protein to improve glucose and lipid homeostasis, while reducing undesired effects.
- **CTPS1 for controlling immune activation**  
CTPS1 is a key enzyme in the pyrimidine synthesis pathway in lymphocytes, making it a drug target for autoimmune diseases and cancer. Selective inhibitors of CTPS1 hold promise for attenuating lymphocyte proliferation and providing effective treatments for T and B cell-driven diseases. Nimbus is using structure-based and other computational chemistry approaches to identify small molecules that are highly potent inhibitors of CTPS1 with selectivity over CTPS2.
- **Cbl-b for enhancing immune sensitivity in cancer**  
Cbl-b is an E3 ubiquitin ligase that directs the degradation of signaling proteins across a variety of immune cells. Cbl-b is a well-validated immuno-oncology target, given that Cbl-b knockout mice spontaneously reject tumors with enhanced T and NK cell responses, and Cbl-b deficient T cells can be activated in the absence of co-stimulatory signals. Nimbus is pursuing a structure-based approach to designing inhibitors of Cbl-b that can enhance anti-tumor immunity.
- **WRN as a selective approach to targeting MSI-high tumors**  
WRN, a helicase required for DNA replication and repair, is a validated target for treating microsatellite-instability high tumors ("MSI-H tumors"). Pharmacological inhibition of helicases has proven difficult in the past, but WRN is now amenable to structural biology approaches, allowing Nimbus to design both active-site and allosteric inhibitors of WRN that should induce synthetic lethality in tumors with microsatellite instability.

## **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. The company's LLC/subsidiary architecture enables diverse and synergistic partnerships to deliver breakthrough medicines. Nimbus is headquartered in Cambridge, Mass. [www.nimbustx.com](http://www.nimbustx.com)

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