Exo Therapeutics Presents Key Data at FOCIS 2024 Demonstrating the Efficacy of Potent and Selective Exosite-targeted TBK1/STING Inhibitor in Multiple Preclinical Models

- Oral and poster presentations show novel, differentiated properties optimized to progress company's nomination of lead development candidate for the treatment of autoimmune diseases -

- FOCIS recognizes Exo with 2024 Annual Meeting Award for exceptional research and posters of merit -

Cambridge, Mass., June 20, 2024 – Exo Therapeutics, Inc., a company developing a pipeline of drug candidates that target exosites, unique small-molecule binding pockets that are distal to traditional active and allosteric sites, thereby reprogramming enzyme activity for precise and robust therapeutic effect, today presented a poster and oral presentation on its preclinical program targeting TBK1/STING interaction of the cGAS-STING pathway at the 24th Annual Meeting of the Federation of Clinical Immunology Societies (FOCIS 2024) in San Francisco.

Data presented in both the poster and oral presentation show that the company has identified potent, selective exosite-targeted TBK1/STING inhibitors, demonstrated efficacy across preclinical models and optimized properties towards development candidate nomination. FOCIS also recognized Exo with the 2024 Annual Meeting Award for exceptional research and posters of merit for the Company's poster and oral presentation.

"Exo's data look very promising, particularly the targeting of both interferon-beta and NF-kB pathways by your molecule," said Mary K. Crow, M.D., Physician-in-Chief Emeritus at Hospital for Special Surgery and Professor of Medicine at Weill Cornell Medical College. "There is a great need to define the role of the TBK1/STING pathway in Systemic Lupus Erythematosus (SLE) and other autoimmune diseases. I hope Exo's development program can soon move forward into patients with their interesting drug!"

Exo's goal is to expand the druggable universe with exosite-specific molecules that enable a new, tailored way to target and reprogram enzymes. Historically, active-site inhibitors have failed because of inadequate selectivity of their inhibitory activity, leading to off-target effects and poor therapeutic indices. Moreover, molecules focused on active or allosteric sites typically inhibit the full functionality of proteins, which can direct both beneficial and harmful effects. In

contrast, TBK1/STING exosite inhibitors have the promise of mitigating the unwanted effects while providing therapeutic benefit.

The presentations detailed Exo's novel TBK1 exosite inhibitors that disrupt recruitment by STING for downstream activation of type-1 interferon and NF-κB responses. More specifically, TBK1 exosite inhibitors selectively inhibit the TBK1-STING axis while sparing non-disease relevant housekeeping functions of the kinase, which will be more likely to offer superior efficacy and an improved therapeutic window versus traditional approaches. The company also shared findings from rational and structure-based drug discovery efforts that demonstrated identification of a series of selective TBK1 exosite inhibitors with potent binding affinities that translate into nanomolar inhibition of IFNβ in THP1 cells and primary human cell types.

Additionally, orally bioavailable TBK1 exosite inhibitors were evaluated in both *in vivo* and *ex vivo* models to inhibit proximal and distal pharmacodynamic markers upon stimulation with a STING agonist. Treatment with TBK1 exosite inhibitors caused a dramatic reduction of pro-inflammatory cytokines including IFNβ, CXCL-10, CXCL-9 and IFIT1 in a pathway-driven model, the *TREX-1* null mouse. Additionally, Exo's TBK1 exosite inhibitors have shown robust effects in SLE and Scleroderma patient samples.

Most notably, when assessed for activity in SLE patient-derived human whole blood and PBMC, TBK1 exosite inhibitors robustly suppressed pathway activation. Similarly, upon activation of cGAS-STING-TBK1 pathway, TBK1 exosite inhibitors inhibited cytokine production in disease-relevant skin inflammatory models, fibroblasts and keratinocytes.

Poster Details

Title: A Novel Inhibitor of cGAS-STING-TBK1 Pathway with Broad Application in Autoimmune Diseases
Date: Wednesday, June 19, 2024, 7:30 AM - 7:30 PM
Poster Number: W102
Location: San Francisco Marriott Marquis – Salon 9, Lower B2 Level

Oral Presentation Details

Title: A Novel Inhibitor of cGAS-STING-TBK1 Pathway with Broad Application in Autoimmune Diseases
Date: Wednesday, June 19, 2024, 4:15 PM - 4:30 PM
Presenter: Bhavatarini Vangamudi, Ph.D.

About Exo Therapeutics
Exo Therapeutics is a small molecule drug discovery and development company co-founded by Professors David R. Liu, Alan Saghatelian, and Juan Pablo Maianti with a pioneering technology to address intractable pharmaceutical targets. By leveraging the company's ExoSight™ platform, Exo is developing a deep pipeline of potent drug candidates that bind exosites, distal

and unique binding pockets that have the potential to reprogram enzyme activity for precise and robust therapeutic effect. Through this specific and selective approach to challenging targets, the company's team of world-class researchers is unlocking breakthrough therapeutics in inflammation, oncology and a broad range of other diseases. For more information, visit www.exo-therapeutics.com.

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