Scenic Biotech Announces *Nature* Publication on the Discovery of Drug Target PLA2G15, a Modifier in Lysosomal Disease

- **In collaboration with a Stanford University research team, Scenic Biotech identified and characterized PLA2G15 as a novel target in lysosomal storage diseases**

Amsterdam, the Netherlands, May 07, 2025 – Scenic Biotech, a pioneer in the field of modifier therapies for severe diseases, today announced a publication in *Nature* covering data on the discovery of PLA2G15 as a target for its lead program in neuro- and metabolic diseases. The publication, titled "PLA2G15 is a BMP Hydrolase and its Targeting Ameliorates Lysosomal Disease", is the result of an ongoing collaboration with the team of Dr. Monther Abu-Remaileh at Stanford University. The study identified the lysosomal phospholipase PLA2G15 as an important modulator of bis(monoacylglycerol)phosphate (BMP) levels, which are known to be altered in many rare, but also common neurodegenerative diseases. The data demonstrate that inhibiting PLA2G15 can significantly improve the disease course in a well-established model for Niemann-Pick type C (NPC), a lysosomal storage disorder also referred to as juvenile Alzheimer's. Scenic Biotech is currently advancing preclinical studies for its lead candidate, a small-molecule inhibitor targeting PLA2G15, for the treatment of neurometabolic diseases such as NPC, Batten Disease and Frontotemporal Lobar Degeneration (FTLD).

"BMP plays an integral role in promoting lysosomal function including lipid degradation and cholesterol trafficking, however, little is known about BMP degradation," said **Monther Abu-Remaileh, PhD, Assistant Professor of Chemical Engineering and of Genetics at Stanford University and co-author of the paper.** "The data published in *Nature* highlight that inhibition of PLA2G15 boosts BMP levels in cells as well as in animal models. BMP is deregulated in a multitude of diseases and has long been thought to be resistant to degradation by lysosomal enzymes. We now show that PLA2G15 can hydrolyze BMP, and importantly, that inhibition of the enzyme presents a promising therapeutic approach."

"The publication in *Nature* is both a validation and a demonstration of the power of our platform that uses human haploid cells to discover disease-relevant targets in various therapeutic areas including our focus areas of neuro- and metabolic diseases," added **Vincent Blomen, PhD, Senior Director of Discovery Sciences at Scenic Biotech and co-author of the paper**. "We demonstrate that targeting PLA2G15 improves neurodegeneration, spleen and liver damage, as well as neurological symptoms and survival in NPC mice. However, we believe this novel drug target has potential in the treatment of other neurodegenerative diseases beyond NPC that are still lacking disease-modifying therapies. With this in mind, we are developing our lead small-molecule inhibitor candidate and are advancing towards IND-enabling studies and aim to proceed to first-in-human studies thereafter."

The publication in *Nature* can be accessed via this link.

About Scenic Biotech
Scenic Biotech is advancing modifier therapy, a radical new approach to treating genetic disorders. Instead of targeting the primary disease-causing mutation, modifier therapy seeks to rebalance health by acting on another gene that can improve or in some cases even bypass the disease impact, leading to a therapeutic effect. Our robust pipeline, derived from our proprietary Cell-Seq platform, includes small molecule programs that are wholly owned. In addition, our platform is leveraged

through strategic collaborations with multinational pharmaceutical leaders. By unlocking new pathways in the genome, Scenic Biotech is developing a range of modifier therapies to help patients.

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