



Wave Life Sciences Announces Publication of Paper in Nature Biotechnology Establishing the Importance of Stereochemical Purity in Oligonucleotide Drug Design

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 22, 2017-- Wave Life Sciences Ltd. (NASDAQ:WVE), a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases, today announced the publication of a new paper in the September issue of *Nature Biotechnology*. The paper describes a breakthrough method to produce antisense oligonucleotide (ASO) therapeutics with high stereochemical purity as well as rational drug design to control pharmacologic properties in nucleic acid therapeutics drug development more broadly. This publication of Wave's stereopure chemistry platform represents a significant scientific advancement for the oligonucleotide field.

The paper, entitled "Control of phosphorothioate stereochemistry substantially increases the efficacy of antisense oligonucleotides," details a proprietary synthesis process developed by Wave. By applying this method, Wave was able to overcome previous barriers to the scalable synthesis of stereochemically pure oligonucleotides.

"These findings represent a breakthrough in the nucleic acid field," said Chandra Vargeese, Ph.D., head of Drug Discovery at Wave Life Sciences. "This paper outlines early foundational principles discovered by Wave to engage RNase H1 that can be applied to any ASO sequence. We have demonstrated that stereochemistry plays a central role in oligonucleotide drug design, with the potential to improve stability, duration of activity and specificity. With continued advancements in our proprietary synthesis process, we have developed a highly efficient manufacturing system that may allow for these key findings to translate into next generation nucleic acid therapeutics. We continue to leverage these initial findings to further build our knowledge base and expand our platform capabilities beyond antisense, including our ongoing work in exon skipping, single stranded RNAi and other modalities."

Wave's researchers synthesized rationally designed stereopure isomers of mipomersen, an FDA approved drug comprised of 524,288 stereoisomers. These researchers demonstrated that phosphorothioate stereochemistry substantially impacts the pharmacologic properties of ASOs. Furthermore, their work identified a stereochemical code that can be rationally designed in the stereopure ASOs that promotes targeted RNA cleavage by RNase H1, and that provides a more durable response in mice than is achieved by stereorandom ASOs. Wave's research also demonstrated that this stereochemical code improved pharmacologic properties both with mipomersen and with a second sequence (conjugated with GalNAc) that targets APOC3. This stereochemical platform provides a foundation for Wave's current pre-clinical and clinical programs, including two recently initiated trials in Huntington's disease (PRECISION-HD1 and PRECISION-HD2).

"These findings provide a powerful demonstration of Wave's stereopure oligonucleotide platform and its potential to rationally design therapies targeting currently untreatable genetic conditions," said Greg Verdine, founder, board member of Wave Life Sciences. "The ability for the first time to exert precise, synthetically programmable control over the chemistry and stereochemistry of ASOs, and the pharmacologic benefits observed for stereochemical optimization as demonstrated in this paper, offer a compelling basis for Wave's novel approach toward advancing safer and more effective nucleic acid therapies."

About Wave Life Sciences

Wave Life Sciences is a biotechnology company focused on delivering transformational therapies for patients with serious, genetically-defined diseases. Our chemistry platform enables the creation of highly specific, well characterized oligonucleotides designed to deliver superior efficacy and safety across multiple therapeutic modalities. Our pipeline is initially focused on neurological disorders and extends across several other therapeutic areas.

Forward Looking Information

This press release contains forward-looking statements, including statements relating to the significance of the paper; the importance of the paper's findings in the field of nucleic acid therapeutics; the distinguishing features of Wave's drug development platform and the potential benefits thereof. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will" and similar expressions, and are based on current beliefs and expectations. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including risks and uncertainties associated with Wave's stereopure chemistry platform, the drug development and regulatory approval process; and the commercialization, development and acceptance of therapies with new technologies, as well as other risks and uncertainties that are described in the Risk Factors section of Wave's most recent annual or quarterly report filed with the U.S. Securities and Exchange Commission. Any forward-looking statements speak only as of the date of this press release and the parties assume no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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