Translatability of miR-29 PD Biomarkers from Preclinical Models to Mechanistic Proof of Concept in an MRG-201 Clinical Trial

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Abstract

Objective: The objective of this study was to identify a set of translational biomarkers from preclinical studies and utilize those biomarkers to assess the pharmacodynamics Assessment of MRG-201, a novel antifibrotic oligonucleotide drug in a Phase 1 clinical trial.

Method: Preclinical studies in human fibroblasts, mouse and rat were performed at Northwestern University. A MRG-201 Administered via Intradermal Injection in NHV Part B Part C Part D

Results: miR-29 is an anti-fibrotic miRNA whose expression is downregulated in multiple fibrotic indications including in cutaneous scars and keloids. Its restoration of miR-29 expression in a skin wound or at the site of an excised scar could have a therapeutic benefit by reducing scarring and/or preventing scar regrowth. An oligonucleotide mimic of miR-29b (MRG-201) and an inhibitor in mouse skin wounds and intact skin to identify a set of miR-29 PD biomarkers in the skin. Studies in rats and rabbits as well as in vitro in human skin fibroblasts confirmed that these PD biomarkers are conserved across species. MRG-201 was then evaluated in a Phase 1 double-blinded within-patient randomized double-blinded, placebo-controlled trial: M, W, F, M, W, F

Conclusion: These findings demonstrate that the miR-29 target genes identified in mouse, rat and rabbit serve as translational biomarkers for assessment of pharmacodynamic activity of MRG-201 in human clinical trials. Use of these PD biomarkers enabled detection of drug activity and mechanistic Proof of Concept of MRG-201 in its first Phase 1 clinical trial in normal healthy volunteers. Furthermore, PD biomarker modulation was shown to correlate with target engagement.

Disclosures

Author(s) of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

► No financial relationships

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