

## A singular focus on cholesterol metabolism modulators

### Cyclodextrin (CD) : Cholesterol Metabolism Modulators (CMMs)

- ✓ CDs are composed of glucose units in a ring structure, which can host cholesterol within the ring and significantly increase its solubility.
- ✓ CDs can normalize dysregulated cholesterol metabolism and mediate cholesterol efflux via the LXR-ABCA1 axis and other pathways.
- Hydroxypropyl-β-CD(HPβCD), a derivative of βCD, is in clinical trials for Alzheimer's disease, Niemann-Pick Type C, and familiar hypercholesterolemia.

#### Problem

- HPβCD is known to induce ototoxicity and other adverse events.
- ✓ Cholesterol removal from the plasma membrane and its disruption is known as the main cause of ototoxicity.



# ABCA1-mediated cholesterol efflux HDL Extracellular Intracellular

## Solution

 RN-005 is cross-linked HPγCD, which exhibits minimal cholesterol removal from the plasma membrane and superior cholesterol solubilization.

Preferential interaction of RN-005 with non-membrane cholesterol



### Safety and efficacy

- RN-005 does not induce ototoxicity at 8,000 mg/kg whereas HPβCD induces complete hearing loss in mice.
- RN-005 has shown therapeutic efficacy in varying disease models including diabetic kidney disease (DKD), atherosclerosis, and Alzheimer's disease (AD).
- RN-005 provides a much wider therapeutic window compared to HPβCD, implying its great potential to allow safe application in varying cholesterol-driven diseases.



### Pipeline

 We are developing novel CD-based drug candidates for various cholesterol-driven diseases

Program	Discovery	Optimization	Preclinical	Clinical
Diabetic kidney disease				
Focal segmental glomerulosclerosis				
Alzheimer's disease				
Niemann-Pick Type C				
Atherosclerosis				
Cancer				

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