Results from the Phase 2 Study of Cemdisiran in Adult Patients with IgA Nephropathy

### Summary
- Monthly subcutaneous dose of cemdisiran led to a clinically meaningful reduction in 24-hour UPCR observed at Week 32 relative to placebo – 37.4% reduction in UPCR at Week 32 relative to placebo – 31.8% of patients treated with cemdisiran (n=12.5% of placebo-treated patients) achieved ≥50% reduction in UPCR at Week 32

### Introduction
- IgAN is the most common type of glomerulonephritis – ~2.5 out of 100,000 individuals are affected each year, with some racial and ethnic variations
- High-grade proteinuria, particularly persistent proteinuria, is a strong risk factor for CKD progression
- IgAN is the most common type of glomerulonephritis
- Treatment options are currently limited for patients with IgAN; management strategies aim to reduce proteinuria and control hypertension – The majority of ISRs were mild and transient; peripheral edema was reported as mild and not related to cemdisiran

### Methods
- **Patient Population**
  - Primary – IgAN with hematuria (≥1 g/24 h)
  - Persistent proteinuria (≥1 g/24 h)
  - Stable optimal treatment
  - No recent steroid or other immunosuppressive therapy (≥6 months)
- **Study Visits**
  - Week 0
  - Week 4
  - Week 8
  - Week 16
  - Week 32
- **Study Endpoints**
  - **Primary Endpoints**
    - Change from baseline in 24-hour UPCR
    - Change from baseline in spot UPCR as measured by random urine sample
    - Incidence of AEs
  - **Secondary Endpoints**
    - Change from baseline in eGFR
    - Change from baseline in renal damage and inflammation markers
    - Change from baseline in complement activity

### Results
- **Demographic and Baseline Disease Characteristics**
  - Race, n (%)
    - Asian
    - Other
    - BMI, mean (SD) (kg/m²)
    - Mean (SD) 24-hour UPCR (g/g) values were 1.8 (1.2) in the cemdisiran group and 2.0 (0.8) in the placebo group.
  - Time since diagnosis, median (IQR) (years)
  - Systolic blood pressure, mean (SD) (mmHg)
    - 116.1 (7.2)
  - Diastolic blood pressure, mean (SD) (mmHg)
    - 76.0 (10.4)
  - 24-hour UMP, mean (SD) (g/day)
    - 2.9 (1.3)
  - 24-hour UPCR, mean (SD) (g/day)
    - 31.4 (9.1)
  - eGFR, mean (SD) (mL/min/1.73 m²)
    - 68.0 (12.9)
  - No ACEi or ARB received
    - 1 (11.1)
- **Change from Baseline in 24-hour UPCR**
  - No ACEi or ARB received
    - 1 (11.1)
  - No treatment discontinuation
    - 0

### Discussion
- Cemdisiran is a subcutaneously administered, investigational RNAi therapeutic that inhibits hepatic production of C5 and is in development for the treatment of complement-mediated diseases
- Demonstrated rapid and robust C5 suppression and an acceptable safety profile in healthy subjects
- The majority of ISRs were mild and transient; peripheral edema was reported as mild and not related to cemdisiran

### Acknowledgments
- Thank you to the patients, their families, investigators, study staff, and collaborators for their continued participation in the cemdisiran Phase 2 IgAN study.